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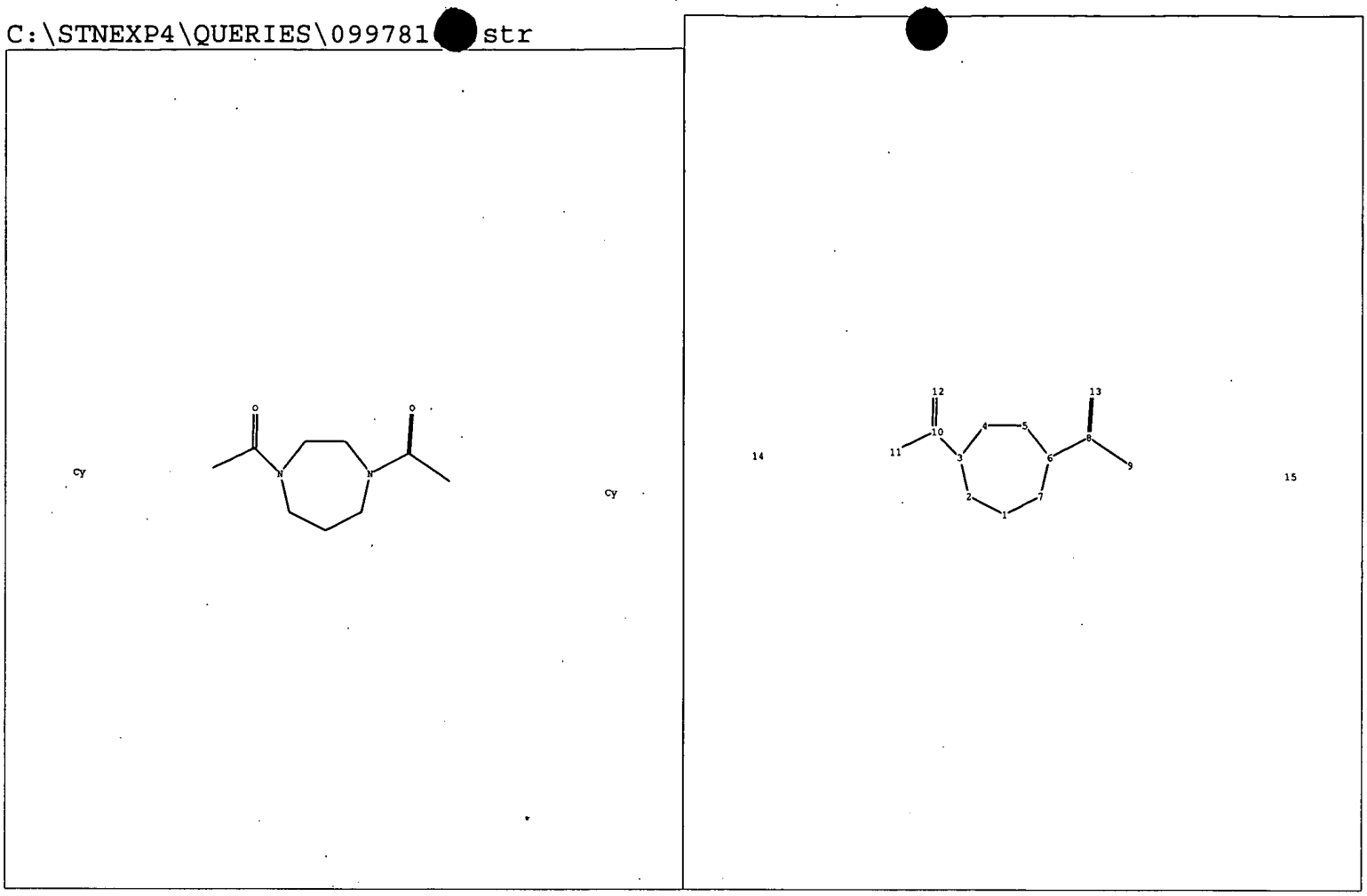

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ring nodes :
1 2 3 4 5 6 7
ring/chain nodes :
9 11
chain bonds :
3-10 6-8 8-9 8-13 10-11 10-12
ring bonds :
1-2 1-7 2-3 3-4 4-5 5-6 6-7
exact/norm bonds :
1-2 1-7 2-3 3-4 3-10 4-5 5-6 6-7 6-8 8-13 10-12
exact bonds :
8-9 10-11

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:CLASS 9:CLASS
10:CLASS 11:CLASS 12:CLASS 13:CLASS 14:Atom 15:Atom

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=> d his

     (FILE 'HOME' ENTERED AT 14:49:07 ON 28 JUL 2003)

     FILE 'REGISTRY' ENTERED AT 14:49:12 ON 28 JUL 2003
L1             STRUCTURE UPLOADED
L2             QUE L1
L3          13 S L2
L4         270 S L2 SSS FUL

     FILE 'CAPLUS' ENTERED AT 14:50:04 ON 28 JUL 2003
L5          39 S L4

=> d l2
L2 HAS NO ANSWERS
L1             STR
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

Structure attributes must be viewed using STN Express query preparation.
L2             QUE  ABB=ON  PLU=ON  L1


=> d ibib abs hitstr 1-39
```

L5 ANSWER 1 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:472347 CAPLUS
DOCUMENT NUMBER: 139:32514
TITLE: HIV integrase inhibitors and their use in treatment of HIV infection
INVENTOR(S): Walker, Michael A.; Banville, Jacques; Remillard, Roger; Plamondon, Serge
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 129 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003049690	A2	20030619	WO 2002-US39092	20021206

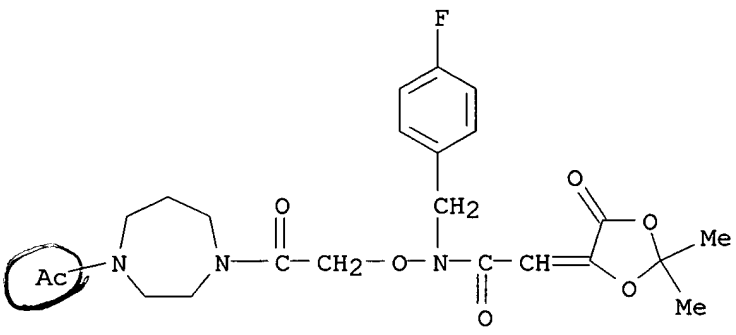
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-339674P P 20011212
OTHER SOURCE(S): MARPAT 139:32514

AB The present invention relates to the inhibition of HIV integrase, and to the treatment of AIDS or ARC by administering compd. R1CH2N(B1)OR2 (R1 = (substituted)aryl, C1-6-alkylaryl, C1-6-alkyl-O-aryl, C1-6-alkyl-SOn-aryl and n = 0,1,2; R2= H, alkyl, cycloalkyl, haloalkyl, aryl, heteroaryl, etc.; B1 = C(:O)C:C(OH)C(:O)OR11 or the 1,3-dioxolan based on this structure, C(:O)CH2C(:O)C(:O)OR11, C(OH):CHC(:O)C(:O)OR11; R11 = H, aryl, heteroaryl, alkylaryl, alkylheteroaryl, etc.), or a tautomer, pharmaceutically acceptable salt, solvate, or prodrug thereof. Thus, 3-[(4-fluorobenzyl)methoxycarbamoyl]-2-hydroxyacrylic acid was synthesized and tested for bioactivity. This compd. exhibited 96% inhibition of recombinant HIV virus expressing luciferase in cell culture at 1.6 .mu.M.

IT **543732-13-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(HIV integrase inhibitors and their use in treatment of HIV infection)

RN 543732-13-4 CAPLUS
CN Acetamide, N-[2-(4-acetylhexahydro-1H-1,4-diazepin-1-yl)-2-oxoethoxy]-2-(2,2-dimethyl-5-oxo-1,3-dioxolan-4-ylidene)-N-[(4-fluorophenyl)methyl]-(9CI) (CA INDEX NAME)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Me
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CH2
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CH
O

L5 ANSWER 2 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:274751 CAPLUS
DOCUMENT NUMBER: 138:297610
TITLE: 1-Methyl carbapenem derivatives as antibacterials
INVENTOR(S): Kawamoto, Isao; Shitaji, Yasuo; Oya, Tetsu
PATENT ASSIGNEE(S): Sankyo Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 31 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2003104893	A2	20030409	JP 2002-215922	20020725

PRIORITY APPLN. INFO.: JP 2001-226893 A 20010727
OTHER SOURCE(S): MARPAT 138:297610
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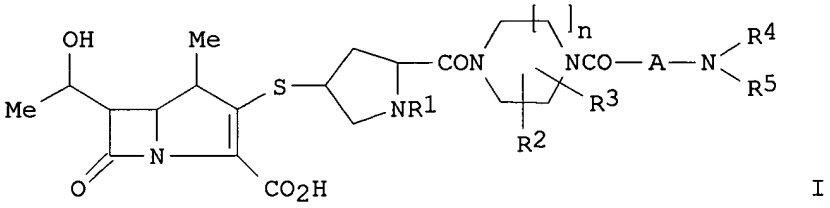


I

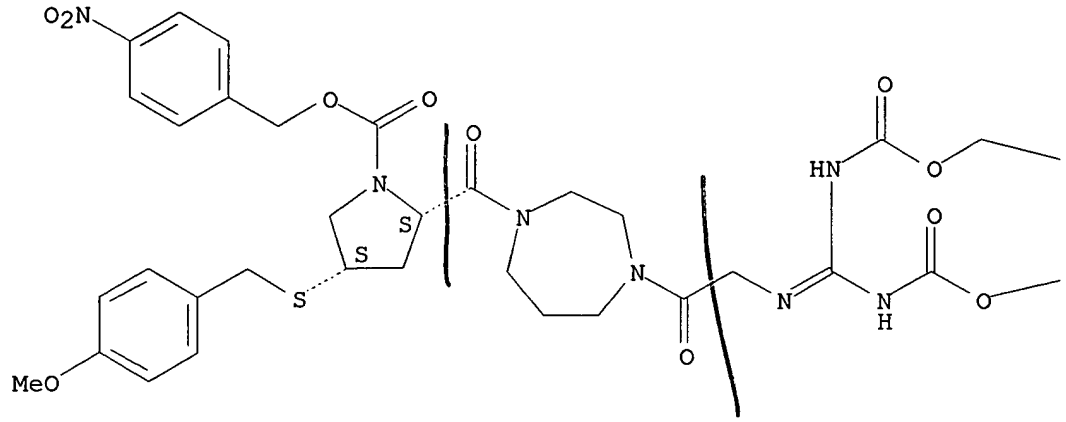
AB 1-Me carbapenem derivs. (I; R1 = C1-6 alkyl, etc.; R2, R3, R4 = H, etc.; R5 = -C(=NH)R6, with R6 = amino, etc.; n = 0-2; A = C1-8 alkylene, etc.) and their prodrugs and pharmacol. acceptable salts are claimed as antibacterials. I were prepd., and their antibacterial activities were tested in vitro. Formulation examples of injections, capsules, and tablets were also given.

IT **353495-75-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(1-Me carbapenem derivs. as antibacterials)

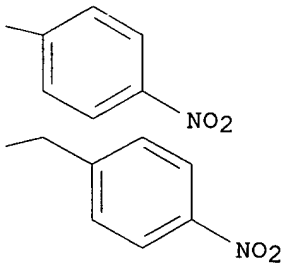
RN 353495-75-7 CAPLUS
CN 1-Pyrrolidinecarboxylic acid, 2-[[4-[[[bis[[[(4-nitrophenyl)methoxy]carbonyl]amino]methylene]amino]acetyl]hexahydro-1H-1,4-diazepin-1-yl]carbonyl]-4-[[(4-methoxyphenyl)methyl]thio]-, (4-nitrophenyl)methyl ester, (2S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



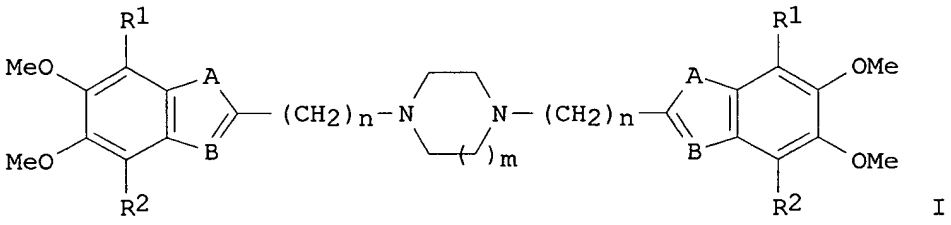
PAGE 1-B



L6 ANSWER 3 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:22849 CAPLUS
DOCUMENT NUMBER: 138:73280
TITLE: Preparation of cyclic diamine compounds having fused-ring groups as cell adhesion inhibitors
INVENTOR(S): Kodama, Tatsuhiko; Tamura, Masahiro; Oda, Toshiaki; Yamazaki, Yukiyoshi; Nishikawa, Masahiro; Doi, Takeshi; Kyotani, Yoshinori
PATENT ASSIGNEE(S): Kowa Co., Ltd., Japan
SOURCE: PCT Int. Appl., 98 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003002532	A1	20030109	WO 2002-JP6487	20020627
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003060461	A1	20030327	US 2001-893696	20010629

PRIORITY APPLN. INFO.: US 2001-893696 A 20010629
OTHER SOURCE(S): MARPAT 138:73280
GI



I

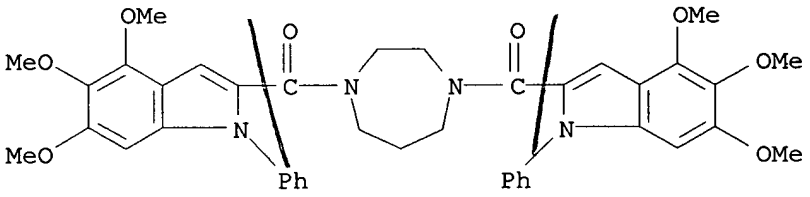
AB Cyclic diamine compds. such as N,N'-bis(naphthylalkyl)-, N,N'-bis(quinolylmethyl)-, N,N'-bis(quinazolinylmethyl)-, N,N'-bis(indolinylmethyl)-, N,N'-bis(benzimidazolylmethyl)-, N,N'-bis(benzothiazolylmethyl)piperazine, and -homopiperazine derivs. represented by the general formula (I), acid-addn. salts thereof, or hydrates of both [wherein R1 and R2 are each hydrogen or methoxy, with the proviso that when R2 is hydrogen, R1 is methoxy, while when R2 is methoxy, R1 is hydrogen; A is oxygen, sulfur, CH:CH, CH:N, or NR3 (wherein R3 is hydrogen, lower alkyl, hydroxy-lower alkyl, lower alkoxy-lower alkyl, aryl, or aryl-lower alkyl); B is nitrogen, CH, or CR4 (wherein R4 is hydrogen, lower alkyl, hydroxy-lower alkyl, lower alkoxy-lower alkyl, aryl, or aryl-lower alkyl); m is 1 or 2; and n is a no. of 1 to 5] are prepd. The above compds., salts, and hydrates exhibit inhibitory activity

against cell adhesion and are useful as drugs for the prevention or treatment of diseases caused by cell adhesion and/or cell infiltration which are selected from allergy, asthma, rheumatic diseases, arteriosclerosis, and inflammation. Thus, 200 mg 2-chloromethyl-5,6,7-trimethoxybenzothiazole and 37 mg homopiperazine were dissolved in DMF and stirred with K2CO3 at room temp. for 5 h to give N,N'-bis[(5,6,7-trimethoxybenzothiazol-2-yl)methyl]homopiperazine (II). II at 1 .mu.M in vitro inhibited the binding of human monocyte/ histiocyte-derived U937 cell to human umbilical venous endothelial cells (HUVEC) stimulated by IL-1.beta. and TNF.alpha. by 79 and 64%, resp. A capsule, tablet, and injection formulation contg. N,N'-[(5,6,7-trimethoxynaphthalene-2-yl)]piperazine were described.

IT **481074-76-4P**, 1,4-Bis[(1-phenyl-4,5,6-trimethoxyindol-2-yl)carbonyl]homopiperazine
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of cyclic diamine compds. having fused-ring groups as cell adhesion inhibitors for prevention or treatment of allergy, asthma, rheumatic diseases, arteriosclerosis, and inflammation)

RN 481074-76-4 CAPLUS

CN 1H-1,4-Diazepine, hexahydro-1,4-bis[(4,5,6-trimethoxy-1-phenyl-1H-indol-2-yl)carbonyl]- (9CI) (CA INDEX NAME)



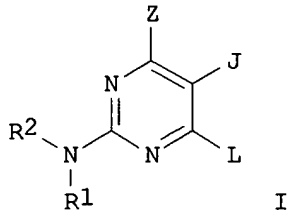
REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 4 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:977601 CAPLUS
DOCUMENT NUMBER: 138:55972
TITLE: Preparation of pyrimidine inhibitors of phosphodiesterase (PDE) 7
INVENTOR(S): Guo, Junqing; Barbosa, Joseph; Pitts, William John; Carlsen, Marianne; Quesnelle, Claude; Dodier, Marco
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 165 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

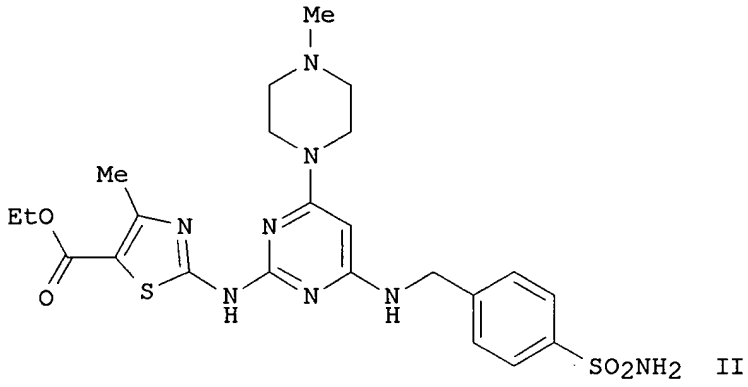
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002102313	A2	20021227	WO 2002-US19097	20020617
WO 2002102313	A3	20030403		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-299287P P 20010619
US 2002-355141P P 20020208
US 2002-368752P P 20020329
OTHER SOURCE(S): MARPAT 138:55972
GI



I



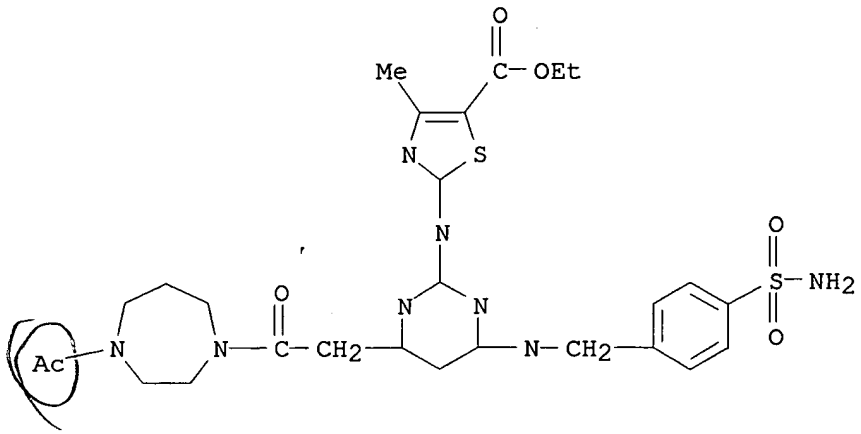
II

AB The title compds. [I; R1 = H, alkyl; R2 = (un)substituted heteroaryl, heterocyclyl, aryl, aryl fused to heteroaryl or heterocyclyl; Z = halo, alkyl, aryl, etc.; J = H, halo, alkyl, etc.; L = H, halo, haloalkyl, etc.], phosphodiesterase 7 (PDE 7) inhibitors (including both selective inhibitors of PDE 7, and dual inhibitors of PDE 7 and phosphodiesterase 4) which are useful in treating T-cell mediated diseases, were prepd. E.g., a multi-step synthesis of II, starting from 2-imino-4-thiobiuret and Et 2-chloroacetoacetate, was given.

IT **479230-92-7P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of pyrimidine inhibitors of phosphodiesterase (PDE) 7)

RN 479230-92-7 CAPLUS

CN 5-Thiazolecarboxylic acid, 2-[[4-[2-(4-acetylhexahydro-1H-1,4-diazepin-1-yl)-2-oxoethyl]-6-[[[4-(aminosulfonyl)phenyl]methyl]amino]-2-pyrimidinyl]amino]-4-methyl-, ethyl ester (9CI) (CA INDEX NAME)



*** FRAGMENT DIAGRAM IS INCOMPLETE ***

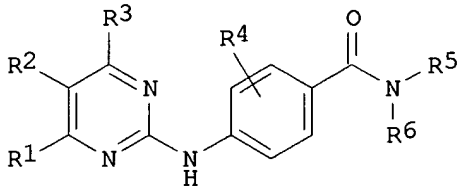
L5 ANSWER 5 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:449662 CAPLUS
DOCUMENT NUMBER: 137:33310
TITLE: Preparation of anilinopyrimidines as IKK inhibitors
INVENTOR(S): Kois, Adam; MacFarlane, Karen J.; Satoh, Yoshitaka; Bhagwat, Shripad S.; Parnes, Jason S.; Palanki, Moorthy S. S.; Erdman, Paul E.
PATENT ASSIGNEE(S): Signal Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 194 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002046171	A2	20020613	WO 2001-US46403	20011205
WO 2002046171	A3	20030123		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2002020195	A5	20020618	AU 2002-20195	20011205

PRIORITY APPLN. INFO.: US 2000-251816P P 20001206
WO 2001-US46403 W 20011205
OTHER SOURCE(S): MARPAT 137:33310
GI



I

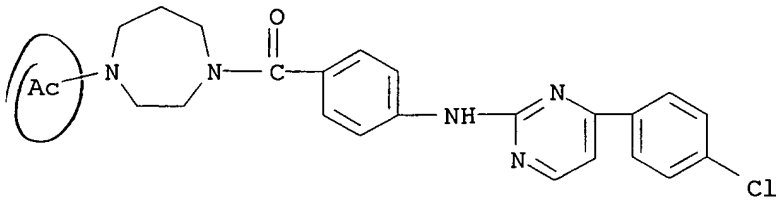
AB The title compds. [I; R1 = (un)substituted (hetero)aryl; R2 = H; R3 = H, alkyl; R4 = halo, OH, alkyl, alkoxy; R5, R6 = R8, (CH2)aCOR9, (CH2)aCO2R9, etc.; or NR5R6 = (un)substituted heterocycle; R8, R9 = H, alkyl, aryl, etc.; a = 0-4] having activity as inhibitors of IKK, particularly IKK-2, were prepd. E.g., a multi-step synthesis of I [R1 = 4-ClC6H4; R2-R6 = H] having an IC50 of .ltoreq. 1 .mu.M in the IKK-2 enzyme assay, was given. Such compds. I have utility in the treatment of a wide range of conditions that are responsive to IKK inhibition. Thus, methods of treating such conditions are also disclosed, as are pharmaceutical compns. contg. one or more compds. of the above compds.

IT **434947-09-8P**

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of anilinopyrimidines as IKK inhibitors)

RN 434947-09-8 CAPLUS

CN 1H-1,4-Diazepine, 1-acetyl-4-[4-[[4-(4-chlorophenyl)-2-pyrimidinyl]amino]benzoyl]hexahydro- (9CI) (CA INDEX NAME)



L5 ANSWER 6 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:449661 CAPLUS
DOCUMENT NUMBER: 137:33309
TITLE: Preparation of anilinopyrimidines as JNK pathway inhibitors
INVENTOR(S): Kois, Adam; MacFarlane, Karen J.; Satoh, Yoshitaka; Bhagwat, Shripad S.; Parnes, Jason S.; Palanki, Moorthy S. S.; Erdman, Paul E.
PATENT ASSIGNEE(S): Signal Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 199 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002046170	A2	20020613	WO 2001-US46402	20011205
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002027214	A5	20020618	AU 2002-27214	20011205

PRIORITY APPLN. INFO.: US 2000-251904P P 20001206
WO 2001-US46402 W 20011205
OTHER SOURCE(S): MARPAT 137:33309
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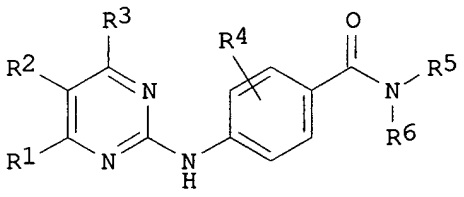
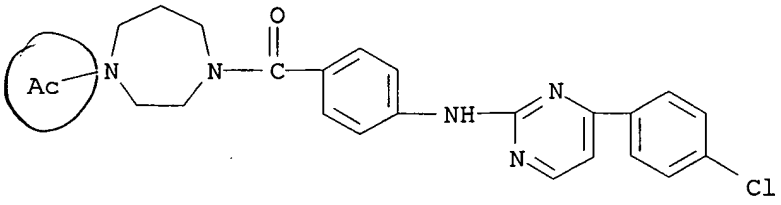


I

AB The title compds. [I; R1 = (un)substituted (hetero)aryl; R2 = H; R3 = H, alkyl; R4 = halo, OH, alkyl, alkoxy; R5, R6 = R8, (CH2)aCOR9, (CH2)aCO2R9, etc.; or NR5R6 = (un)substituted heterocycle; R8, R9 = H, alkyl, aryl, etc.; a = 0-4] having activity as inhibitors of the JNK pathway, were prepd. E.g., a multi-step synthesis of I [R1 = 4-ClC6H4; R2-R6 = H] having an IC50 of .ltoreq. 10 .mu.M in the JNK2 assay, was given. Such compds. I have utility in the treatment of a wide range of conditions that are responsive to inhibition of the JNK pathway. Thus, methods of treating such conditions are also disclosed, as are pharmaceutical compns. contg. one or more compds. of the above compds.

IT **434947-09-8P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

(Uses)
(prepn. of anilinopyrimidines as JNK pathway inhibitors)
RN 434947-09-8 CAPLUS
CN 1H-1,4-Diazepine, 1-acetyl-4-[4-[[4-(4-chlorophenyl)-2-pyrimidinyl]amino]benzoyl]hexahydro- (9CI) (CA INDEX NAME)



L5 ANSWER 7 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:107910 CAPLUS
DOCUMENT NUMBER: 136:167282
TITLE: Heterocyclic analgesic compounds, namely N-[1-(1-phenethylpiperidin-3-yl)ethyl]-N-phenylpropionamide and analogs, with activity as opioid receptors, and method of use thereof
INVENTOR(S): Cuny, Gregory D.; Shao, Liming; Hauske, James R.; Heffernan, Michele L. R.; Aquila, Brian M.; Wu, Xinhe; Wang, Fengjiang; Bannister, Thomas D.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 107 pp., Cont.-in-part of U.S. Ser. No. 717,174.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002016337	A1	20020207	US 2001-798803	20010302
WO 2002069895	A2	20020912	WO 2002-US6274	20020301
WO 2002069895	A3	20021031		
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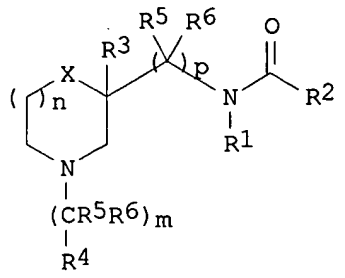
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003069418	A1	20030410	US 2002-121029	20020411

PRIORITY APPLN. INFO.:
US 2000-579398 A2 20000525
US 2000-717174 A2 20001120
US 1999-135721P P 19990525
US 1999-168979P P 19991203
US 2000-195809P P 20000411
US 2001-798803 A 20010302
US 2001-284374P P 20010417

OTHER SOURCE(S): MARPAT 136:167282
GI



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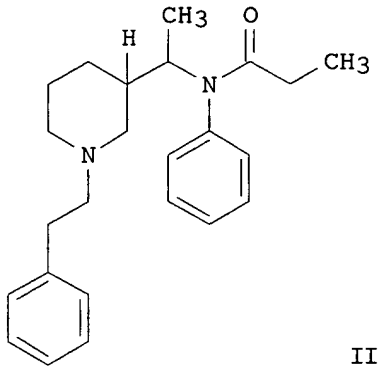

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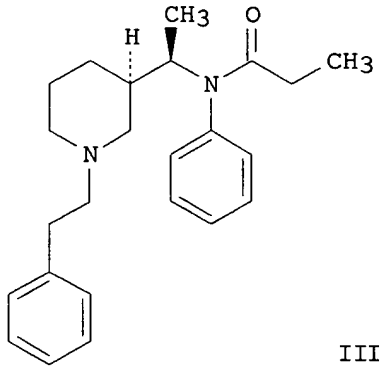


III

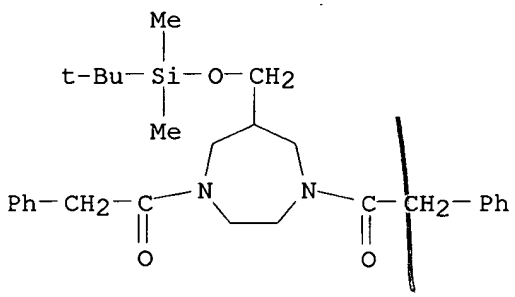
AB One aspect of the invention relates to novel heterocyclic compds. (6 Markush structures given), e.g., I [wherein: m = 1, 2, 3 or 4; n = 1 or 2; p = 1 or 2; R1 = alkyl, aryl, heteroaryl, or cycloalkyl; R2 = H, alkyl, fluoroalkyl, aryl, heteroaryl, or cycloalkyl; R1 and R2 may be connected through a covalent bond; R3 = H, alkyl, aryl, OR2, OC(O)R2CH2OR2, or CO2R2; wherein any 2 instances of R3 may be connected by a covalent tether whose backbone consists of 1, 2, 3, or 4 C atoms; R4 = H, alkyl, aryl, heteroaryl, alkenyl, or cycloalkyl; R5 = H, alkyl, CH2Y, aryl, heteroaryl, F, OR2, or OC(O)R2; R6 = H, alkyl, CH2Y, aryl, heteroaryl, F, OR2, or OC(O)R2; Y = OR2, N(R2)2, SR2, S(O)R2, S(O)2R2, or P(O)(OR2)2; a covalent bond may connect R4 and an instance of R5 or R6 that is attached to the C chain between R4 and the ring N explicitly shown; any 2 geminal or vicinal instances of R5 and R6 may be connected through a covalent bond; X = C(R3)2, O, S, SO, SO2, NR2, NC(O)OR2, or C:O; and the stereochem. configuration at any stereocenter is (R)-, (S)-, or mixed]. A second aspect of the invention relates to the use of the compds. as ligands for various cellular receptors, including opiate receptors, other G-protein-coupled receptors, and ion channels. An addnl. aspect of the invention relates to the use of the compds. as analgesics. A large no. of synthetic and biol. examples are given, including a combinatorial prepn. For instance, 3-(1-hydroxyethyl)piperidine-1-carboxylic acid tert-Bu ester was converted to its mesylate ester, and this reacted with aniline to give 3-[1-(phenylamino)ethyl]piperidine-1-carboxylic acid tert-Bu ester. Amidation of this with propionyl chloride, deprotection of the BOC group with CF3CO2H, and N-alkylation with PhCH2CH2Br, gave the invention compd. II. All 4 enantiomers of II were prepd. by a stereospecific synthesis, and X-ray crystallog. detn. of one enantiomer allowed the abs. stereochem. of its epimer, III, to be assigned. III showed an ED50 of <500 .mu.g/kg (i.v.) in the tail flick assay in rats, which was comparable to fentanyl. The respiratory depression activity (side effect) of 14 invention compds.

was also detd. An orally bioavailable formulation of III was studied in rats. A combinatorial library of 96 compds. I was prepd. from 12 anilines and 8 acid chlorides.

IT **309748-22-9P**, 1,4-Bis(phenylacetyl)-6-[(tert-butyldimethylsilyloxy)methyl]-1,4-diazepane **309748-24-1P**, 1,4-Bis(phenylacetyl)-1,4-diazepane-6-methanol **309748-26-3P**, 1,4-Bis(phenylacetyl)-1,4-diazepane-6-carboxaldehyde **309748-28-5P**, 1,4-Bis(phenylacetyl)-N-phenyl-1,4-diazepane-6-methanamine
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; prepn. of [(phenethylpiperidinyl)ethyl]phenylpropionamides and analogs as analgesics)

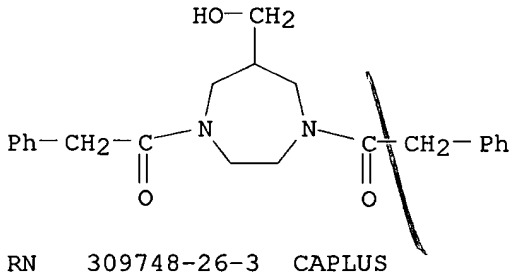
RN 309748-22-9 CAPLUS

CN 1H-1,4-Diazepine, 6-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]hexahydro-1,4-bis(phenylacetyl)- (9CI) (CA INDEX NAME)



RN 309748-24-1 CAPLUS

CN 1H-1,4-Diazepine-6-methanol, hexahydro-1,4-bis(phenylacetyl)- (9CI) (CA INDEX NAME)



RN 309748-26-3 CAPLUS

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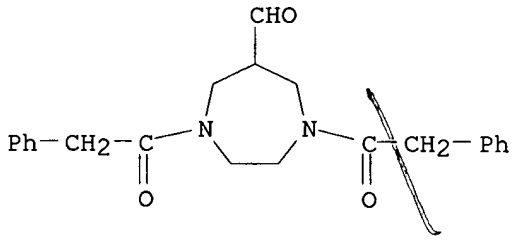
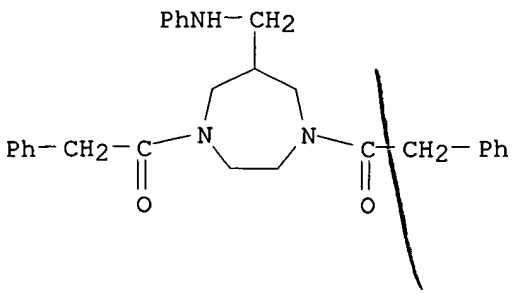


RN 309748-28-5 CAPLUS

CN 1H-1,4-Diazepine-6-methanamine, hexahydro-N-phenyl-1,4-bis(phenylacetyl)-

(9CI) (CA INDEX NAME)

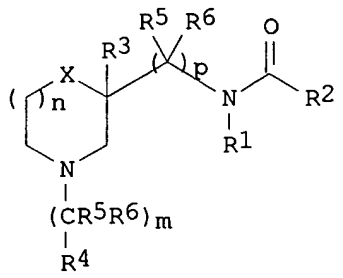


L5 ANSWER 8 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:886067 CAPLUS
DOCUMENT NUMBER: 136:20020
TITLE: Heterocyclic analgesic compounds, namely N-[1-(1-phenethylpiperidin-3-yl)ethyl]-N-phenylpropionamide and analogs, with activity at opioid receptors, and method of use thereof
INVENTOR(S): Cuny, Gregory D.; Shao, Liming; Hauske, James R.; Heffernan, Michele L. R.; Aquila, Brian M.; Wu, Xinhe; Wang, Fengjian; Bannister, Thomas D.
PATENT ASSIGNEE(S): Sepracor, Inc., USA
SOURCE: PCT Int. Appl., 229 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001092226	A1	20011206	WO 2000-US31724	20001120

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-579398 A 20000525
OTHER SOURCE(S): MARPAT 136:20020
GI



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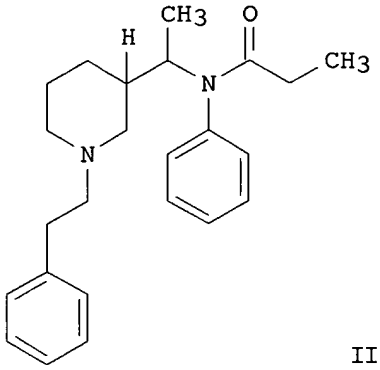

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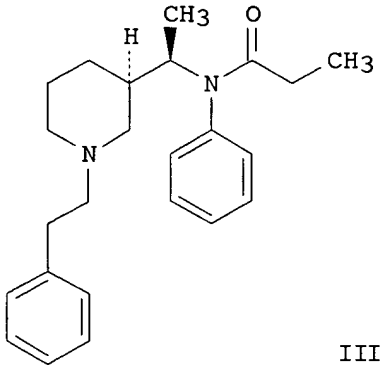


III

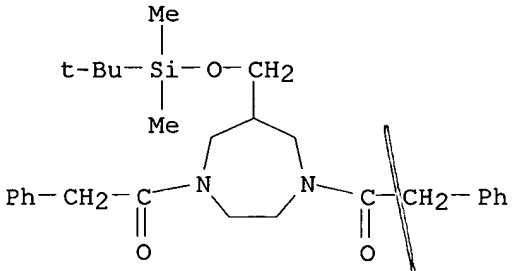
AB One aspect of the invention relates to novel heterocyclic compds. (6 Markush structures given), e.g., I [wherein: m = 1, 2, 3 or 4; n = 1 or 2; p = 1 or 2; R1 = alkyl, aryl, heteroaryl, or cycloalkyl; R2 = H, alkyl, fluoroalkyl, aryl, heteroaryl, or cycloalkyl; R1 and R2 may be connected through a covalent bond; R3 = H, alkyl, aryl, OR2, OC(O)R2CH2OR2, or CO2R2; wherein any 2 instances of R3 may be connected by a covalent tether whose backbone consists of 1, 2, 3, or 4 C atoms; R4 = H, alkyl, aryl, heteroaryl, alkenyl, or cycloalkyl; R5 = H, alkyl, CH2Y, aryl, heteroaryl, F, OR2, or OC(O)R2; R6 = H, alkyl, CH2Y, aryl, heteroaryl, F, OR2, or OC(O)R2; Y = OR2, N(R2)2, SR2, S(O)R2, S(O)2R2, or P(O)(OR2)2; a covalent bond may connect R4 and an instance of R5 or R6 that is attached to the C chain between R4 and the ring N explicitly shown; any 2 geminal or vicinal instances of R5 and R6 may be connected through a covalent bond; X = C(R3)2, O, S, SO, SO2, NR2, NC(O)OR2, or C:O; and the stereochem. configuration at any stereocenter is (R)-, (S)-, or mixed]. A second aspect of the invention relates to the use of the compds. as ligands for various cellular receptors, including opiate receptors, other G-protein-coupled receptors, and ion channels. An addnl. aspect of the invention relates to the use of the compds. as analgesics. A large no. of synthetic and biol. examples are given, including a combinatorial prepn. For instance, 3-(1-hydroxyethyl)piperidine-1-carboxylic acid tert-Bu ester was converted to its mesylate ester, and this reacted with aniline to give 3-[1-(phenylamino)ethyl]piperidine-1-carboxylic acid tert-Bu ester. Amidation of this with propionyl chloride, deprotection of the BOC group with CF3CO2H, and N-alkylation with PhCH2CH2Br, gave the invention compd. II. All 4 enantiomers of II were prepd. by a stereospecific synthesis, and X-ray crystallog. detn. of one enantiomer allowed the abs. stereochem. of its epimer, III, to be assigned. III showed an ED50 of <500 .mu.g/kg (i.v.) in the tail flick assay in rats, which was comparable to fentanyl. The respiratory depression activity (side effect) of 14 invention compds.

was also detd. An orally bioavailable formulation of III was studied in rats. A combinatorial library of 96 compds. I was prepd. from 12 anilines and 8 acid chlorides.

IT **309748-22-9P**, 1,4-Bis(phenylacetyl)-6-[(tert-butyldimethylsilyloxy)methyl]-1,4-diazepane **309748-24-1P**, 1,4-Bis(phenylacetyl)-1,4-diazepane-6-methanol **309748-26-3P**, 1,4-Bis(phenylacetyl)-1,4-diazepane-6-carboxaldehyde **309748-28-5P**, 1,4-Bis(phenylacetyl)-N-phenyl-1,4-diazepane-6-methanamine
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; prepn. of [(phenethylpiperidinyl)ethyl]phenylpropionamides and analogs as analgesics)

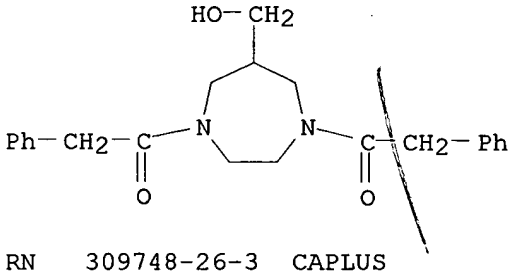
RN 309748-22-9 CAPLUS

CN 1H-1,4-Diazepine, 6-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]hexahydro-1,4-bis(phenylacetyl)- (9CI) (CA INDEX NAME)



RN 309748-24-1 CAPLUS

CN 1H-1,4-Diazepine-6-methanol, hexahydro-1,4-bis(phenylacetyl)- (9CI) (CA INDEX NAME)



RN 309748-26-3 CAPLUS

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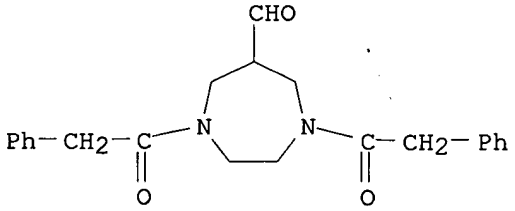

RN 309748-28-5 CAPLUS

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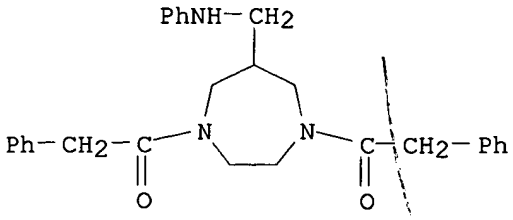
(9CI) (CA INDEX NAME)



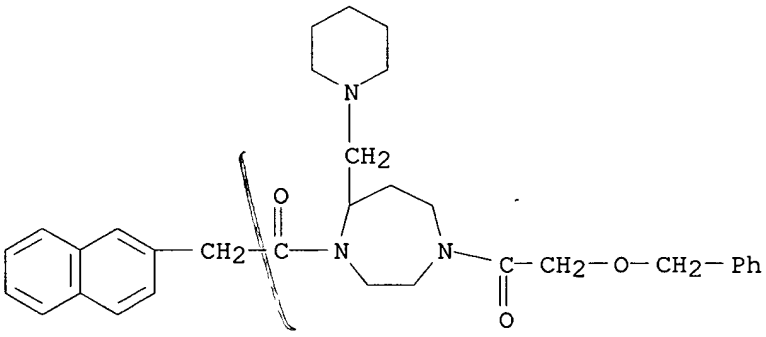
REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 9 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:883263 CAPLUS
DOCUMENT NUMBER: 136:263140
TITLE: Synthesis of 5-substituted hexahydro-1H-1, 4-diazepine analogues
AUTHOR(S): Shen, Jing Shan; Lei, Li Jun; Mao, Hai Fang; Li, Jian Feng; Ji, Ru Yun
CORPORATE SOURCE: Shanghai Institute of Materia Medica, Chinese Academy of Sciences, Shanghai, 200031, Peop. Rep. China
SOURCE: Chinese Chemical Letters (2001), 12(11), 951-954
CODEN: CCLEE7; ISSN: 1001-8417
PUBLISHER: Chinese Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB 5-Substituted hexahydro-1H-1,4-diazepine derivs. were synthesized starting from N,N'-dibenzyl-1, 2-ethylenediamine and Me 2, 4-dibromide butyrate through nucleophilic substitution, redn., chlorination, debenzylation and amidation. Some compds. showed activity as .kappa.-opioid receptor antagonists.

IT **405160-77-2P 405160-78-3P 405160-79-4P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of hexahydro-1H-1,4-diazepine derivs. and their activity as .kappa.-opioid receptor antagonists)

RN 405160-77-2 CAPLUS
CN 1H-1,4-Diazepine, hexahydro-4-(2-naphthalenylacetyl)-1-[(phenylmethoxy)acetyl]-5-(1-piperidinylmethyl)- (9CI) (CA INDEX NAME)



RN 405160-78-3 CAPLUS
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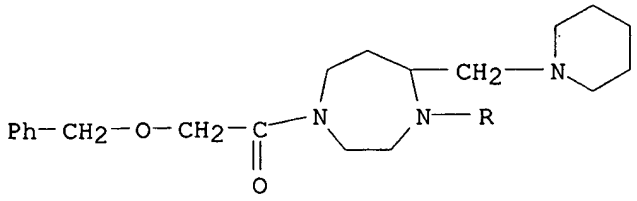

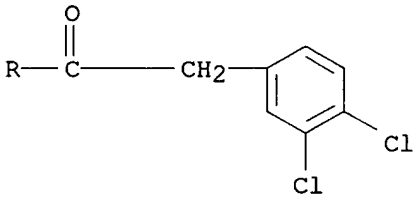

RN 405160-79-4 CAPLUS
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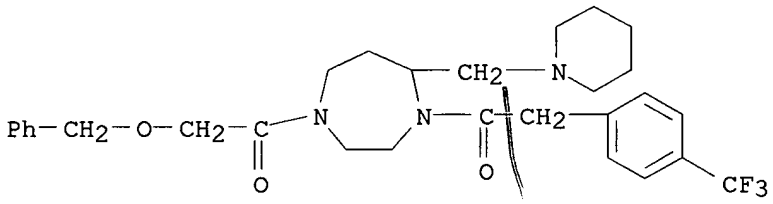

IT **405160-80-7P 405160-82-9P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of hexahydro-1H-1,4-diazepine derivs. and their activity as .kappa.-opioid receptor antagonists)
RN 405160-80-7 CAPLUS
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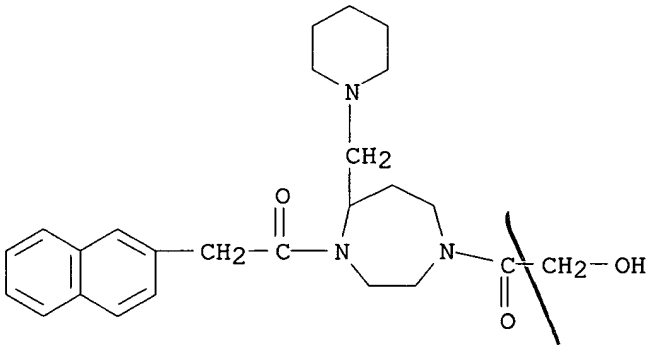
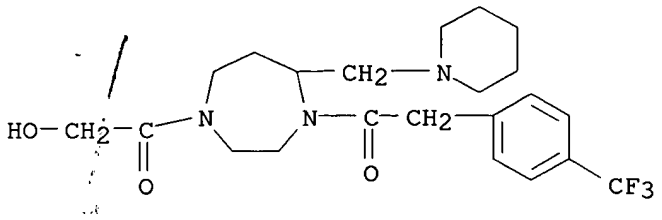
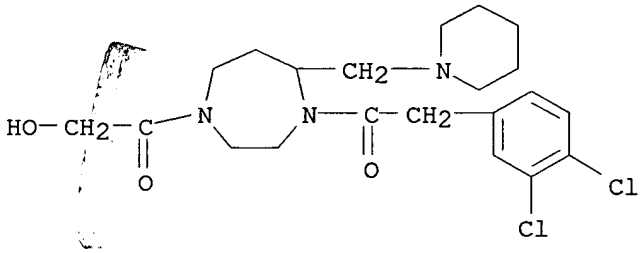


RN 405160-82-9 CAPLUS
CN 1H-1,4-Diazepine, hexahydro-1-(hydroxyacetyl)-5-(1-piperidinylmethyl)-4-[[4-(trifluoromethyl)phenyl]acetyl]- (9CI) (CA INDEX NAME)



IT **405160-81-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of hexahydro-1H-1,4-diazepine derivs. and their activity as .kappa.-opioid receptor antagonists)
RN 405160-81-8 CAPLUS
CN 1H-1,4-Diazepine, 4-[(3,4-dichlorophenyl)acetyl]hexahydro-1-(hydroxyacetyl)-5-(1-piperidinylmethyl)- (9CI) (CA INDEX NAME)

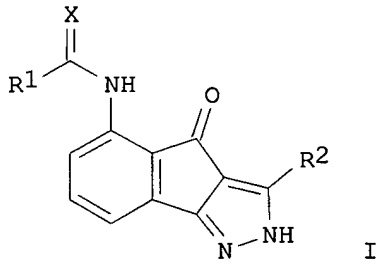


REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

D5 ANSWER 10 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:731369 CAPLUS
DOCUMENT NUMBER: 135:288778
TITLE: Preparation of indeno[1,2-c]pyrazol-4-ones as inhibitors of cyclin dependent kinases
INVENTOR(S): Nugiel, David A.; Carini, David J.; Dimeo, Susan V.; Yue, Eddy W.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 104 pp., Cont.-in-part of U.S. Ser. No. 639,618.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2001027195	A1	20011004	US 2000-731304	20001206
US 6407103	B2	20020618		
US 6413957	B1	20020702	US 2000-639618	20000815
AU 2001012168	A5	20020506	AU 2001-12168	20001020

PRIORITY APPLN. INFO.: US 1998-82476P P 19980421
US 1999-295078 B1 19990420
US 2000-639618 A2 20000815
WO 2000-US28952 A 20001020
OTHER SOURCE(S): MARPAT 135:288778
GI



I

AB The present invention relates to the synthesis of a new class of indeno[1,2-c]pyrazol-4-ones of formula [X = O, S, (un)substituted NH; R1 = H, (un)substituted C1-10 alkyl, C2-10 alkenyl, C2-10 alkynyl, NH2, C3-10 membered carbocyclyl, 3-10 membered heterocycle contg. 1-4 heteroatoms selected from O, N, and S; R2 = H, (un)substituted C1-10 alkyl, C2-10 alkenyl, C2-10 alkynyl, (CF2)mCF3, C3-10 membered carbocyclyl, 3-10 membered heterocycle contg. 1-4 heteroatoms selected from O, N, and S; wherein m = 0, 1-4]. These compds. are potent inhibitors of the class of enzymes known as cyclin dependent kinases, which relate to the catalytic subunits cdk1-9 and their regulatory subunits know as cyclins A-H. This invention also provides a novel method of treating cancer or other proliferative diseases by administering a therapeutically effective amt. of one of these compds. or a pharmaceutically acceptable salt form thereof. Alternatively, cancer or other proliferative diseases can be treated by administering a therapeutically effective combination of one of the compds. of the present invention and one or more other known

anti-cancer or anti-proliferative agents (no data). Thus, hydrogenation of di-Me 3-nitrophthalate over 5% Pd-C in methanol in a Parr shaker at 50 psi for 2 h followed by acetylation with Ac2O in pyridine at 25.degree. for 2 h gave 79% di-Me 3-acetamidophthalate which was treated with NaH in DMF and cyclocondensed with 4-methoxyacetophenone at 90.degree. for 20 min to give 30% 2-(4-methoxybenzoyl)-4-acetamidoindane-2,3-dione. Cyclocondensation of the latter triketone with hydrazine hydrate in the presence of p-TsOH in ethanol under reflux for 2 h gave I (R1 = Me, X = O, R2 = 4-methoxyphenyl).

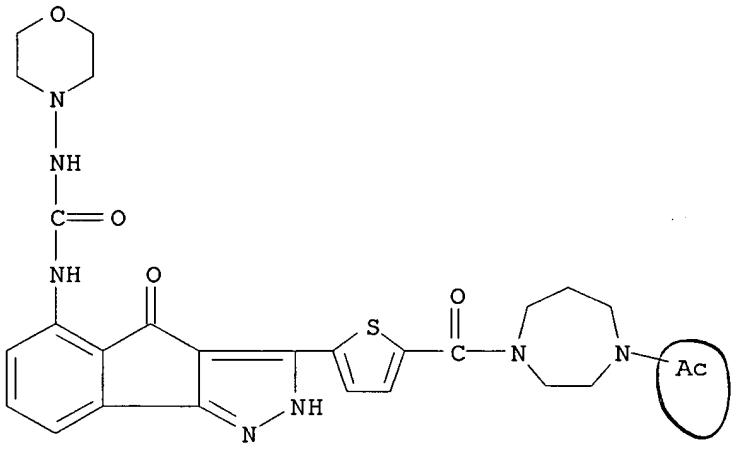
IT **364734-58-7P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

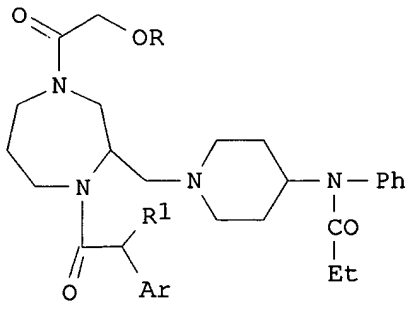
(prepn. of indeno[c]pyrazolones as inhibitors of cyclin dependent kinases)

RN 364734-58-7 CAPLUS

CN 1H-1,4-Diazepine, 1-acetyl-4-[[5-[2,4-dihydro-5-[[(4-morpholinylamino)carbonyl]amino]-4-oxoindeno[1,2-c]pyrazol-3-yl]-2-thienyl]carbonyl]hexahydro- (9CI) (CA INDEX NAME)



L5 ANSWER 11 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:618883 CAPLUS
DOCUMENT NUMBER: 136:5967
TITLE: Synthesis of hexahydro-1H-1,4-diazepine analogues carrying the segment of (1-arylacetamide-2-tertiaryamide)ethane(II)
AUTHOR(S): Shen, Jing-Shan; Lei, Li-Jun; Yan, Tie-Ma; Wei, Min; Ji, Ru-Yun
CORPORATE SOURCE: Shanghai Inst. Materia Medica, The Chinese Academy Science, Shanghai, 200031, Peop. Rep. China
SOURCE: Huaxue Xuebao (2001), 59(8), 1317-1322
CODEN: HHHPA4; ISSN: 0567-7351
PUBLISHER: Kexue Chubanshe
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
OTHER SOURCE(S): CASREACT 136:5967
GI

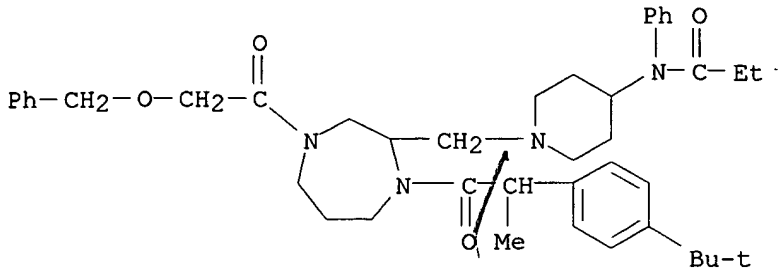


I

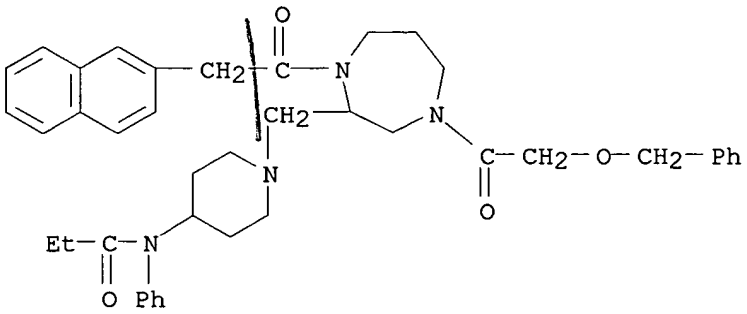
AB Title compds. I (Ar = 4-(CH3)2CHC6H4, 2-naphthyl, 3,4-Cl2C6H3, 3-F3CC6H4; R = C6H5CH2; R1 = H, CH3) were prepd. from 2-methoxycarbonyl-1,4-dibenzyl-1,4-diazepine, 4-(N-phenyl-N-propionyl)aminopiperidine, C6H5COOCH2CO2H, and ArCH2CO2H, trough acylation and amination. Title compds. I (Ar = 4-(CH3)2CHC6H4, 2-naphthyl, 3,4-Cl2C6H3, 3-F3CC6H4; R = H), contg. hydrophilic group, were prepd. through debenzylation of title compds. I (R = C6H5CH2). The products were characterized by IR, EIMS, elementary anal. and 1H NMR. Title compds. I were tested for biol. activities.

IT **375855-23-5P 375855-24-6P 375855-25-7P**
375855-26-8P 375855-27-9P 375855-28-0P
375855-29-1P 375855-35-9P 375855-36-0P
375855-37-1P 375855-38-2P 375855-39-3P
375855-40-6P 375855-41-7P
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(Synthesis of arylacetamidoethylhexahydro-1H-1,4-diazepines as kappa receptor agonists)

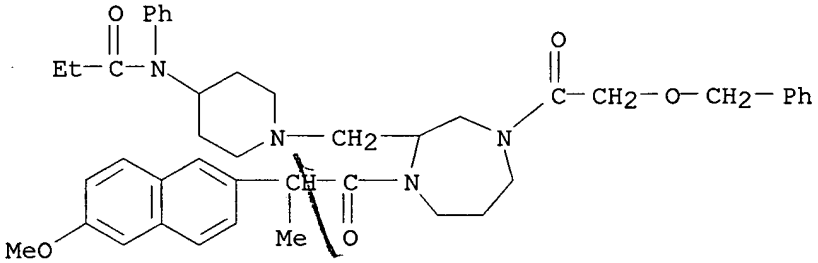
RN 375855-23-5 CAPLUS
CN Propanamide, N-[1-[[1-[2-[4-(1,1-dimethylethyl)phenyl]-1-oxopropyl]hexahydro-4-[(phenylmethoxy)acetyl]-1H-1,4-diazepin-2-yl]methyl]-4-piperidinyl]-N-phenyl- (9CI) (CA INDEX NAME)



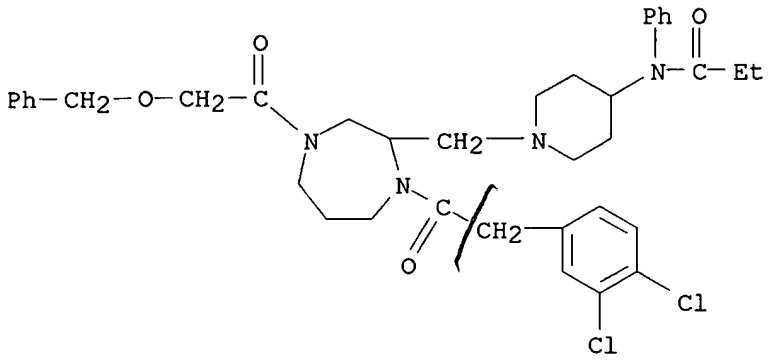
RN 375855-24-6 CAPLUS
CN Propanamide, N-[1-[[hexahydro-1-(2-naphthalenylacetyl)-4-[(phenylmethoxy)acetyl]-1H-1,4-diazepin-2-yl]methyl]-4-piperidinyl]-N-phenyl- (9CI) (CA INDEX NAME)



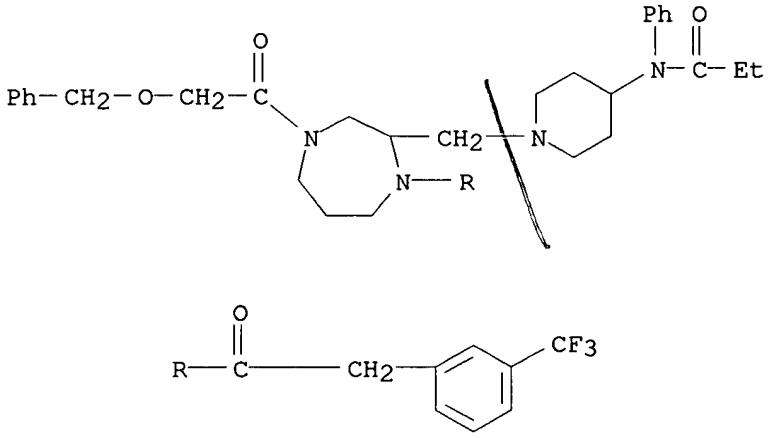
RN 375855-25-7 CAPLUS
CN Propanamide, N-[1-[[hexahydro-1-[2-(6-methoxy-2-naphthalenyl)-1-oxopropyl]-4-[(phenylmethoxy)acetyl]-1H-1,4-diazepin-2-yl]methyl]-4-piperidinyl]-N-phenyl- (9CI) (CA INDEX NAME)



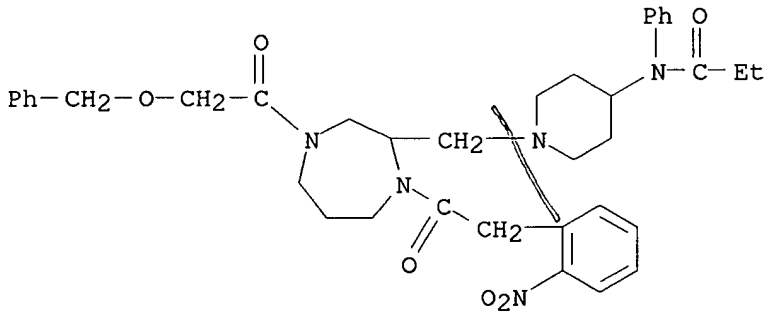
RN 375855-26-8 CAPLUS
CN Propanamide, N-[1-[[1-[(3,4-dichlorophenyl)acetyl]hexahydro-4-[(phenylmethoxy)acetyl]-1H-1,4-diazepin-2-yl]methyl]-4-piperidinyl]-N-phenyl- (9CI) (CA INDEX NAME)



RN 375855-27-9 CAPLUS
CN Propanamide, N-[1-[[hexahydro-4-[(phenylmethoxy)acetyl]-1-[[3-(trifluoromethyl)phenyl]acetyl]-1H-1,4-diazepin-2-yl]methyl]-4-piperidinyl]-N-phenyl- (9CI) (CA INDEX NAME)

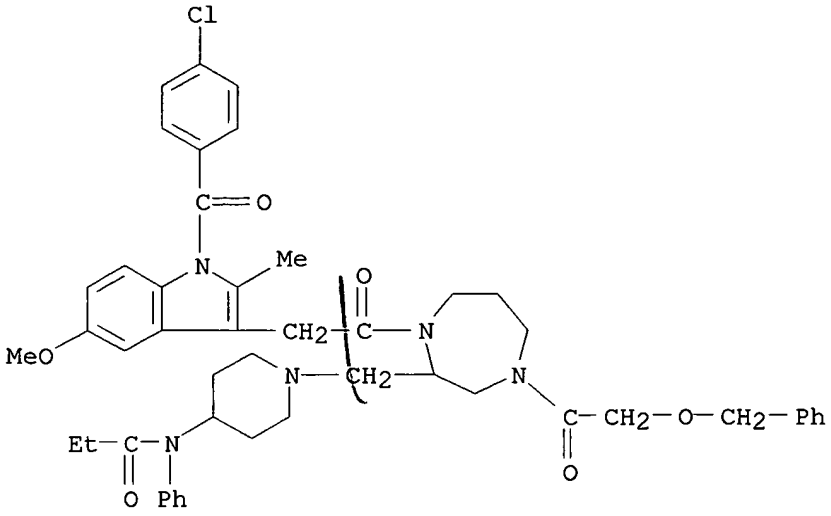


RN 375855-28-0 CAPLUS
CN Propanamide, N-[1-[[hexahydro-1-[(2-nitrophenyl)acetyl]-4-[(phenylmethoxy)acetyl]-1H-1,4-diazepin-2-yl]methyl]-4-piperidinyl]-N-phenyl- (9CI) (CA INDEX NAME)



RN 375855-29-1 CAPLUS

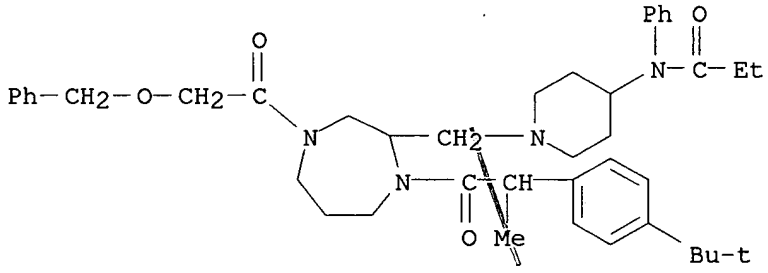
CN Propanamide, N-[1-[[1-[[1-(4-chlorobenzoyl)-5-methoxy-2-methyl-1H-indol-3-yl]acetyl]hexahydro-4-[(phenylmethoxy)acetyl]-1H-1,4-diazepin-2-yl]methyl]-4-piperidinyl]-N-phenyl- (9CI) (CA INDEX NAME)



RN 375855-35-9 CAPLUS
CN Propanamide, N-[1-[[1-[2-[4-(1,1-dimethylethyl)phenyl]-1-oxopropyl]hexahydro-4-[(phenylmethoxy)acetyl]-1H-1,4-diazepin-2-yl]methyl]-4-piperidinyl]-N-phenyl-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

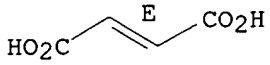
CRN 375855-23-5
CMF C42 H56 N4 O4



CM 2

CRN 110-17-8
CMF C4 H4 O4

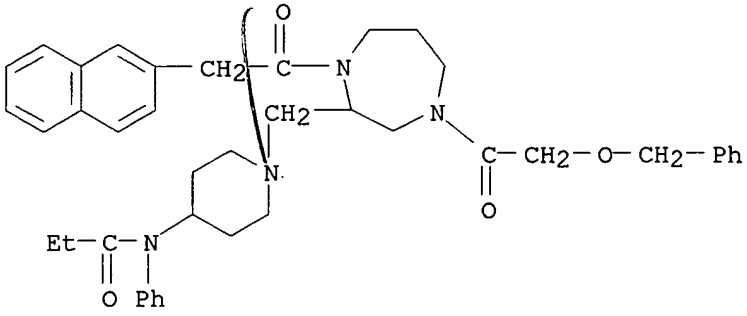
Double bond geometry as shown.



RN 375855-36-0 CAPLUS
CN Propanamide, N-[1-[[hexahydro-1-(2-naphthalenylacetyl)-4-[(phenylmethoxy)acetyl]-1H-1,4-diazepin-2-yl]methyl]-4-piperidinyl]-N-phenyl-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

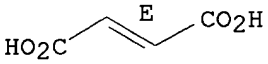
CRN 375855-24-6
CMF C41 H48 N4 O4



CM 2

CRN 110-17-8
CMF C4 H4 O4

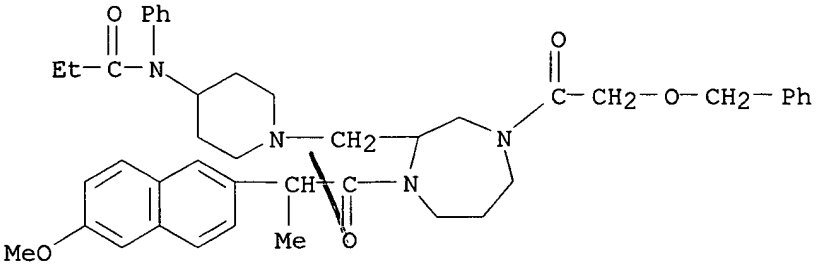
Double bond geometry as shown.



RN 375855-37-1 CAPLUS
CN Propanamide, N-[1-[[hexahydro-1-[2-(6-methoxy-2-naphthalenyl)-1-oxopropyl]-4-[(phenylmethoxy)acetyl]-1H-1,4-diazepin-2-yl]methyl]-4-piperidinyl]-N-phenyl-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

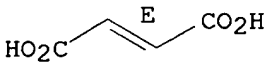
CRN 375855-25-7
CMF C43 H52 N4 O5



CM 2

CRN 110-17-8
CMF C4 H4 O4

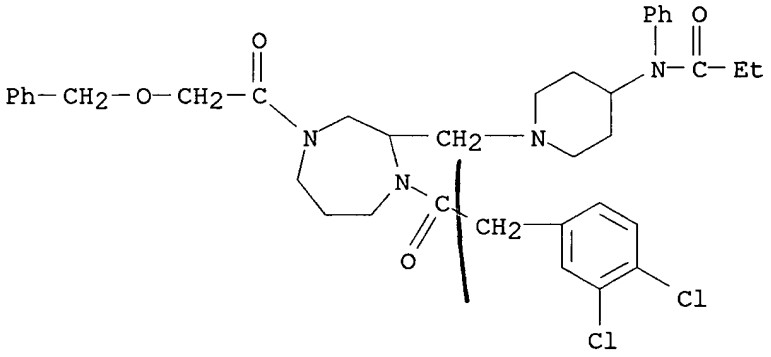
Double bond geometry as shown.



RN 375855-38-2 CAPLUS
CN Propanamide, N-[1-[[1-[(3,4-dichlorophenyl)acetyl]hexahydro-4-[(phenylmethoxy)acetyl]-1H-1,4-diazepin-2-yl]methyl]-4-piperidinyl]-N-phenyl-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

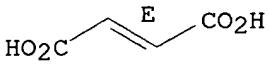
CRN 375855-26-8
CMF C37 H44 Cl2 N4 O4



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.

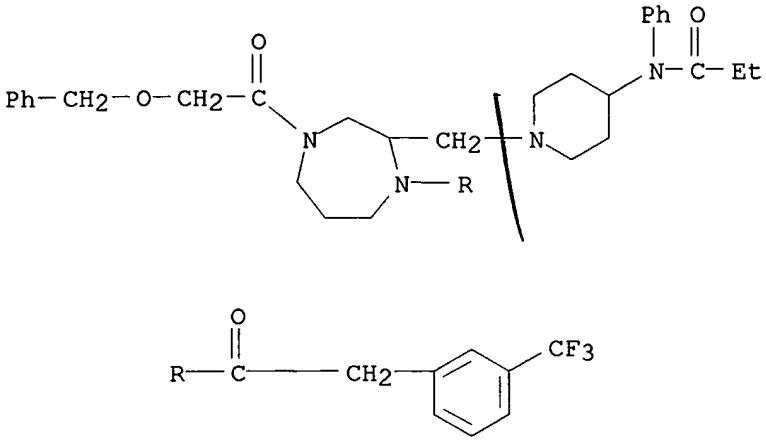


RN 375855-39-3 CAPLUS
CN Propanamide, N-[1-[[hexahydro-4-[(phenylmethoxy)acetyl]-1-[[3-(trifluoromethyl)phenyl]acetyl]-1H-1,4-diazepin-2-yl]methyl]-4-piperidinyl]-N-phenyl-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 375855-27-9

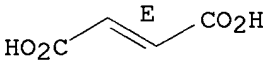
CMF C38 H45 F3 N4 O4



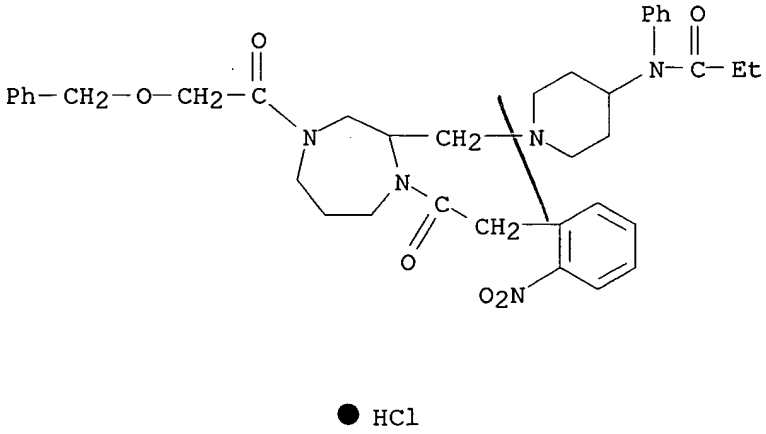
CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



RN 375855-40-6 CAPLUS
CN Propanamide, N-[1-[[hexahydro-1-[(2-nitrophenyl)acetyl]-4-[(phenylmethoxy)acetyl]-1H-1,4-diazepin-2-yl]methyl]-4-piperidinyl]-N-phenyl-, monohydrochloride (9CI) (CA INDEX NAME)



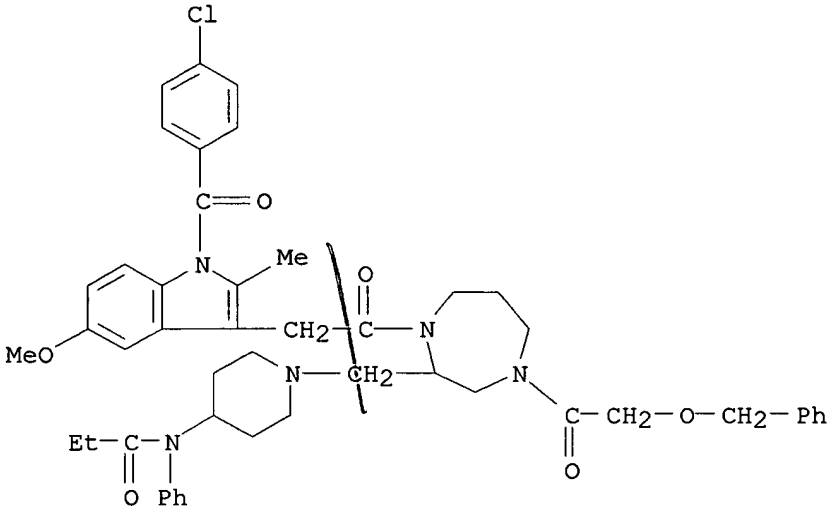
● HCl

RN 375855-41-7 CAPLUS
CN Propanamide, N-[1-[[1-[[1-(4-chlorobenzoyl)-5-methoxy-2-methyl-1H-indol-3-yl]acetyl]hexahydro-4-[(phenylmethoxy)acetyl]-1H-1,4-diazepin-2-yl]methyl]-

4-piperidinyl]-N-phenyl-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

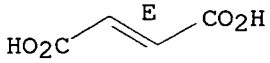
CRN 375855-29-1
CMF C48 H54 Cl N5 O6



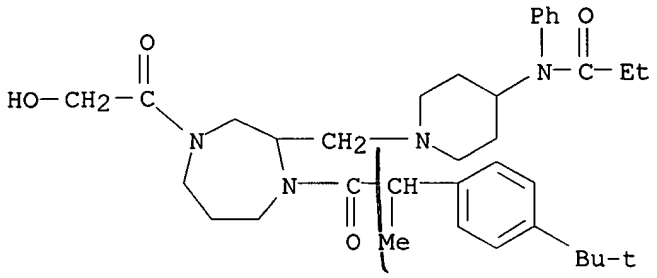
CM 2

CRN 110-17-8
CMF C4 H4 O4

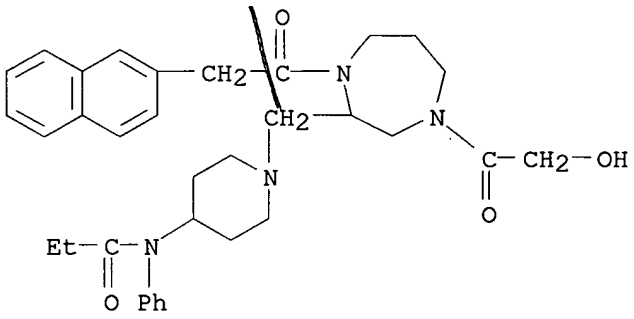
Double bond geometry as shown.



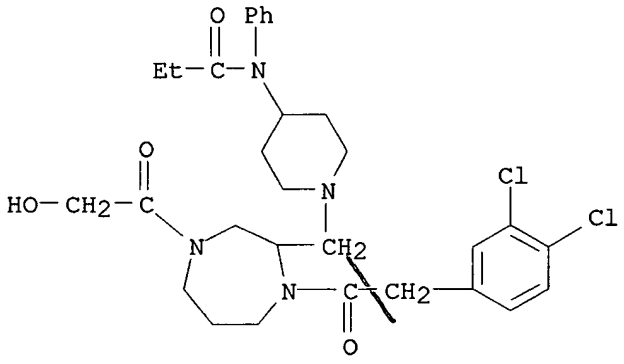
IT **375855-30-4P 375855-31-5P 375855-32-6P**
375855-33-7P 375855-42-8P
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(Synthesis of arylacetamidoethylhexahydro-1H-1,4-diazepines as kappa receptor agonists)
RN 375855-30-4 CAPLUS
CN Propanamide, N-[1-[[1-[2-[4-(1,1-dimethylethyl)phenyl]-1-oxopropyl]hexahydro-4-(hydroxyacetyl)-1H-1,4-diazepin-2-yl]methyl]-4-piperidinyl]-N-phenyl- (9CI) (CA INDEX NAME)



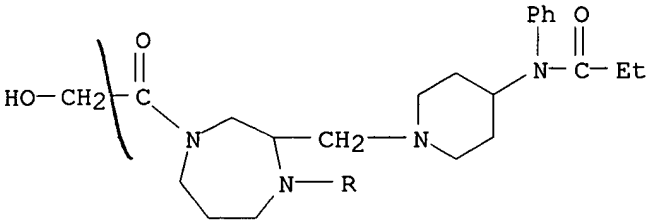
RN 375855-31-5 CAPLUS
CN Propanamide, N-[1-[[hexahydro-4-(hydroxyacetyl)-1-(2-naphthalenylacetyl)-1H-1,4-diazepin-2-yl]methyl]-4-piperidinyl]-N-phenyl- (9CI) (CA INDEX NAME)

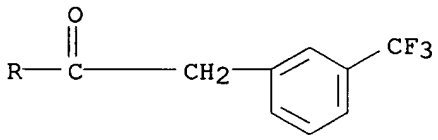


RN 375855-32-6 CAPLUS
CN Propanamide, N-[1-[[1-[(3,4-dichlorophenyl)acetyl]hexahydro-4-(hydroxyacetyl)-1H-1,4-diazepin-2-yl]methyl]-4-piperidinyl]-N-phenyl- (9CI) (CA INDEX NAME)



RN 375855-33-7 CAPLUS
CN Propanamide, N-[1-[[hexahydro-4-(hydroxyacetyl)-1-[[3-(trifluoromethyl)phenyl]acetyl]-1H-1,4-diazepin-2-yl]methyl]-4-piperidinyl]-N-phenyl- (9CI) (CA INDEX NAME)

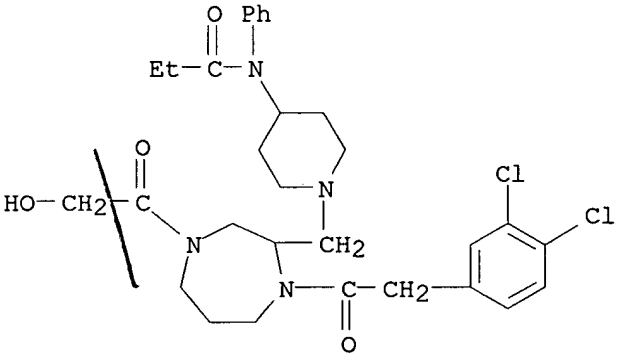




RN 375855-42-8 CAPLUS
CN Propanamide, N-[1-[[1-[(3,4-dichlorophenyl)acetyl]hexahydro-4-(hydroxyacetyl)-1H-1,4-diazepin-2-yl]methyl]-4-piperidinyl]-N-phenyl-, (2E)-2-butenedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

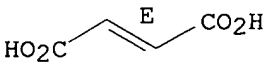
CRN 375855-32-6
CMF C30 H38 Cl2 N4 O4



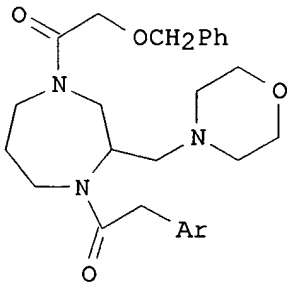
CM 2

CRN 110-17-8
CMF C4 H4 O4

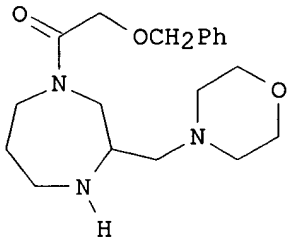
Double bond geometry as shown.



L5 ANSWER 12 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:596267 CAPLUS
DOCUMENT NUMBER: 136:294808
TITLE: Synthesis of hexahydro-1H-1,4-diazepine analogues carrying the segment of (1-arylacetamide-2-tertiary-amide)ethane. I.
AUTHOR(S): Shen, Jing-shan; Lei, Li-jun; Lu, Wei; Li, Jian-feng; Li, Hui-Jun; Ji, Ru-yun
CORPORATE SOURCE: Shanghai Institute of Materia Medica, Chinese Academy of Sciences, Shanghai, 200031, Peop. Rep. China
SOURCE: Hecheng Huaxue (2001), 9(3), 236-240, 246
CODEN: HEHUE2; ISSN: 1005-1511
PUBLISHER: Hecheng Huaxue Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
OTHER SOURCE(S): CASREACT 136:294808
GI



I

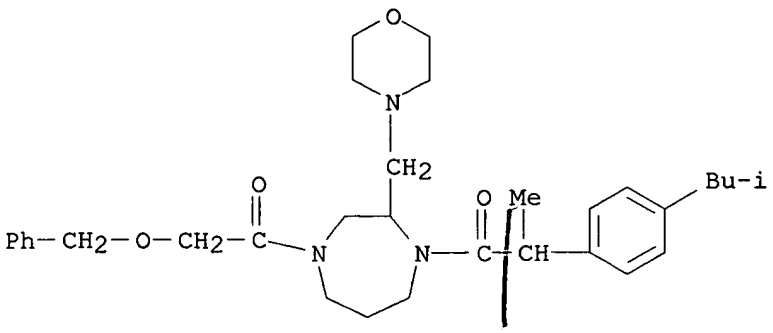


II

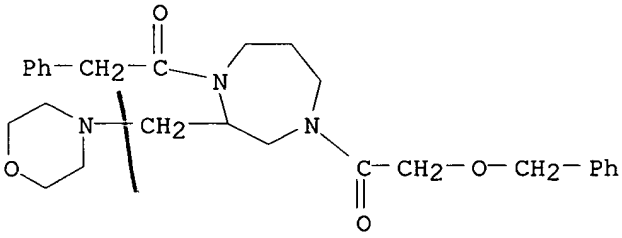
AB Title compds. I (Ar = substituted Ph or indole), potential .kappa.-opioid receptor agonist, were prepd. starting from N,N'-dibenzyl-1,3-propylenediamine and methyl-2,3-dibromopropionate via redn., chlorination, amine substitution, amine debenzylation, single amidation and amidation of compd. II , giving the target compds. with fair to high yield. The structures of the products were characterized by elementary anal., IR, EIMS and 1HNMR. The bioactivity of target compds. are tested in process.

IT **408364-51-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of hexahydro-1H-1,4-diazepine analogs)

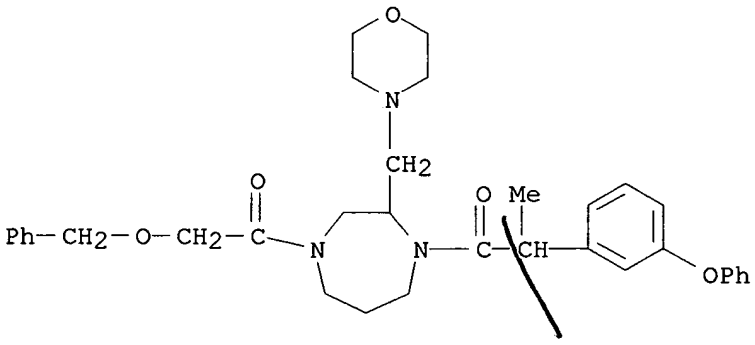
RN 408364-51-2 CAPLUS
CN 1H-1,4-Diazepine, hexahydro-1-[2-[4-(2-methylpropyl)phenyl]-1-oxopropyl]-2-(4-morpholinylmethyl)-4-[(phenylmethoxy)acetyl]- (9CI) (CA INDEX NAME)



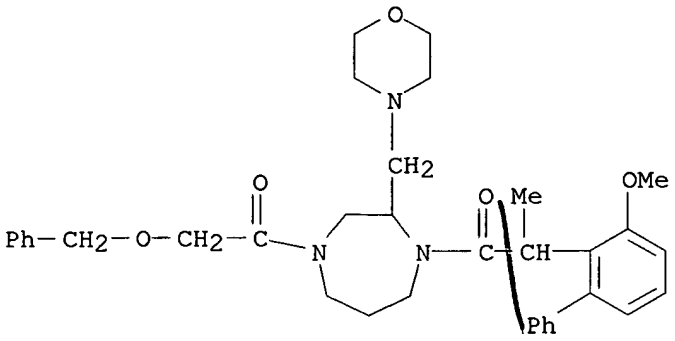
IT **408364-50-1P 408364-52-3P 408364-53-4P**
408364-54-5P 408364-55-6P 408364-56-7P
408364-57-8P 408364-58-9P 408364-62-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis of hexahydro-1H-1,4-diazepine analogs)
RN 408364-50-1 CAPLUS
CN 1H-1,4-Diazepine, hexahydro-2-(4-morpholinylmethyl)-1-(phenylacetyl)-4-[(phenylmethoxy)acetyl]- (9CI) (CA INDEX NAME)



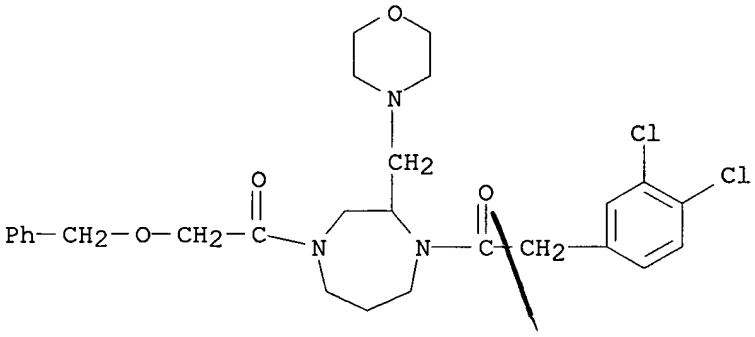
RN 408364-52-3 CAPLUS
CN 1H-1,4-Diazepine, hexahydro-2-(4-morpholinylmethyl)-1-[1-oxo-2-(3-phenoxyphenyl)propyl]-4-[(phenylmethoxy)acetyl]- (9CI) (CA INDEX NAME)



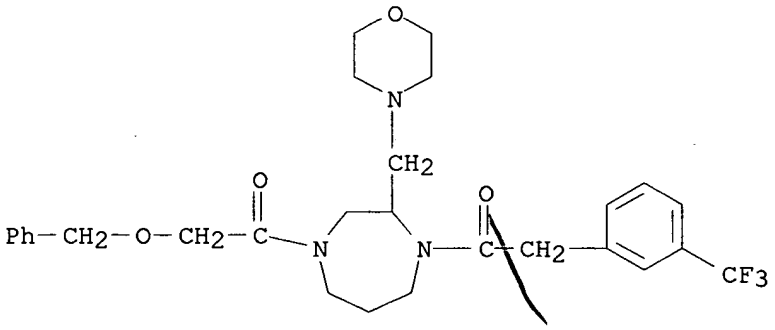
RN 408364-53-4 CAPLUS
CN 1H-1,4-Diazepine, hexahydro-1-[2-(3-methoxy[1,1'-biphenyl]-2-yl)-1-oxopropyl]-2-(4-morpholinylmethyl)-4-[(phenylmethoxy)acetyl]- (9CI) (CA INDEX NAME)



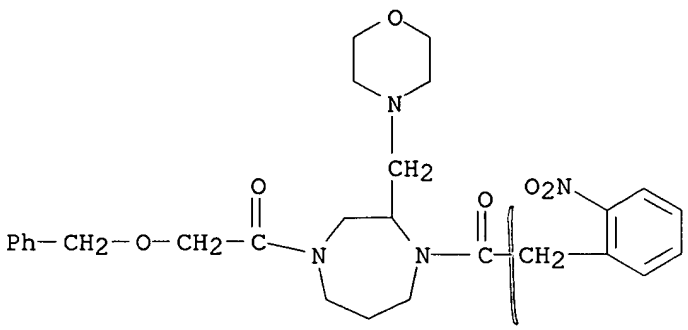
RN 408364-54-5 CAPLUS
CN 1H-1,4-Diazepine, 1-[(3,4-dichlorophenyl)acetyl]hexahydro-2-(4-morpholinylmethyl)-4-[(phenylmethoxy)acetyl]- (9CI) (CA INDEX NAME)



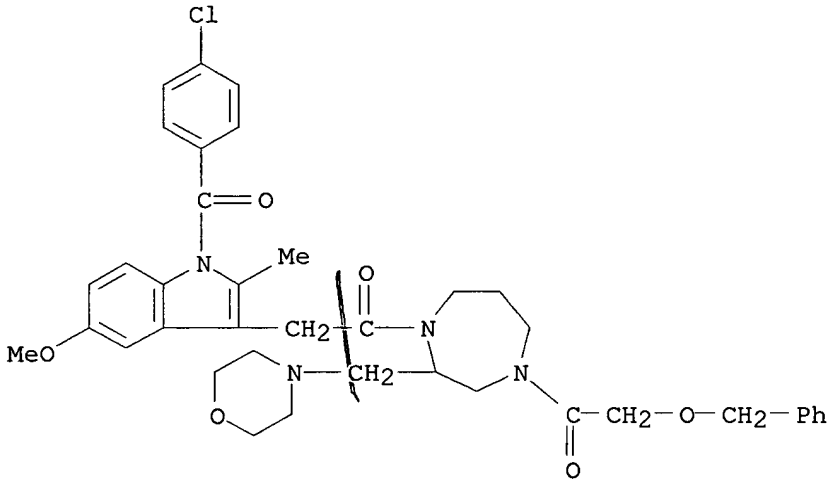
RN 408364-55-6 CAPLUS
CN 1H-1,4-Diazepine, hexahydro-2-(4-morpholinylmethyl)-4-[(phenylmethoxy)acetyl]-1-[[3-(trifluoromethyl)phenyl]acetyl]- (9CI) (CA INDEX NAME)



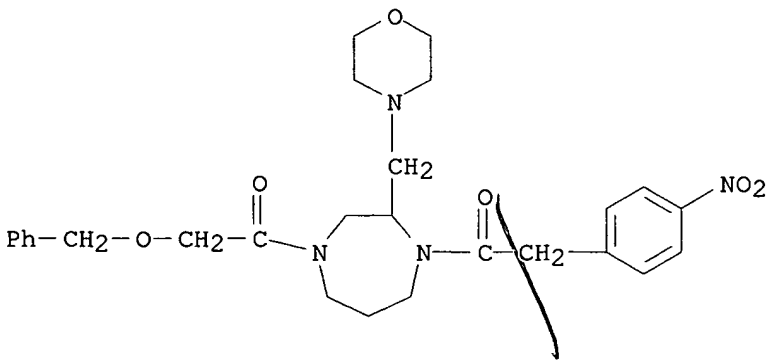
RN 408364-56-7 CAPLUS
CN 1H-1,4-Diazepine, hexahydro-2-(4-morpholinylmethyl)-1-[(2-nitrophenyl)acetyl]-4-[(phenylmethoxy)acetyl]- (9CI) (CA INDEX NAME)



RN 408364-57-8 CAPLUS
CN 1H-Indole, 1-(4-chlorobenzoyl)-3-[2-[hexahydro-2-(4-morpholinylmethyl)-4-[(phenylmethoxy)acetyl]-1H-1,4-diazepin-1-yl]-2-oxoethyl]-5-methoxy-2-methyl- (9CI) (CA INDEX NAME)

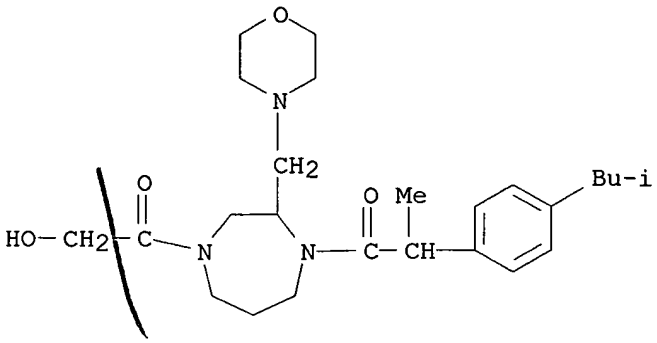


RN 408364-58-9 CAPLUS
CN 1H-1,4-Diazepine, hexahydro-2-(4-morpholinylmethyl)-1-[(4-nitrophenyl)acetyl]-4-[(phenylmethoxy)acetyl]- (9CI) (CA INDEX NAME)



RN 408364-62-5 CAPLUS

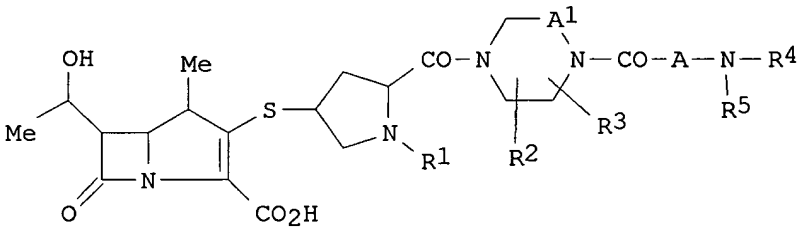
CN 1H-1,4-Diazepine, hexahydro-4-(hydroxyacetyl)-1-[2-[4-(2-methylpropyl)phenyl]-1-oxopropyl]-2-(4-morpholinylmethyl)- (9CI) (CA INDEX NAME)



L5 ANSWER 13 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:581892 CAPLUS
DOCUMENT NUMBER: 135:166736
TITLE: Preparation of 1-methylcarbapenem compounds as antibacterial agents
INVENTOR(S): Kawamoto, Isao; Shimoji, Yasuo; Ohya, Satoshi
PATENT ASSIGNEE(S): Sankyo Co., Ltd., Japan
SOURCE: PCT Int. Appl., 78 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001057041	A1	20010809	WO 2001-JP664	20010131
W: AU, BR, CA, CN, CZ, HU, ID, IL, IN, KR, MX, NO, NZ, PL, RU, US, ZA				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
JP 2001288186	A2	20011016	JP 2001-20858	20010130

PRIORITY APPLN. INFO.: JP 2000-21015 A 20000131
OTHER SOURCE(S): MARPAT 135:166736
GI



I

AB The title compds. I [A1 = (CH2)n; R1 is alkyl or the like; R2 and R3 are each independently hydrogen or the like; R4 is hydrogen or the like; R5 is a group having the formula C(:NH)R6 (wherein R6 is amino or the like); n is 0, 1 or 2; and A is alkylene or the like] are prepd. Compds. of this invention in vitro showed MICs of .ltoreq. 0.01 .mu.g/mL against E. coli NIHJ. Formulations are given.

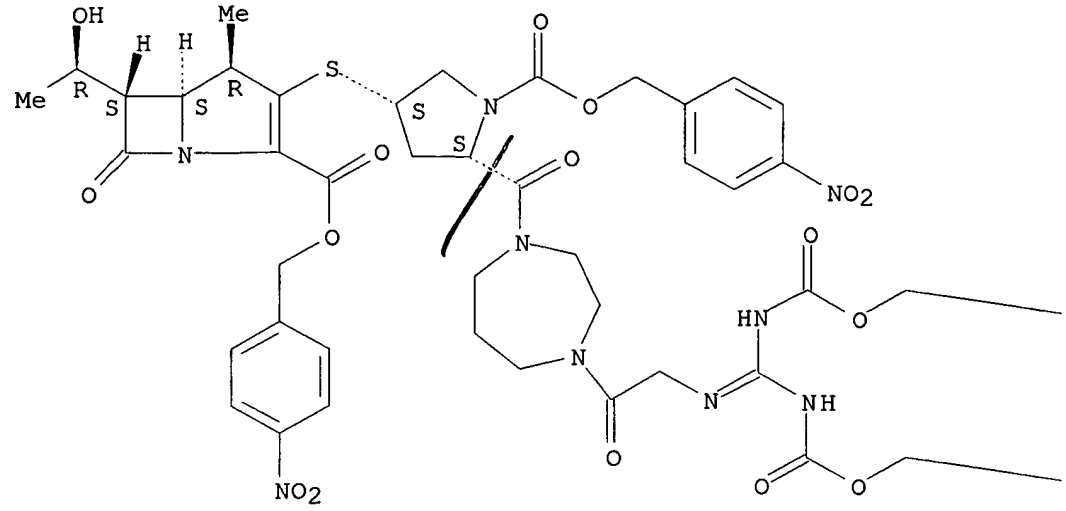
IT **353495-59-7P 353495-60-0P 353495-75-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of methylcarbapenem compds. as antibacterial agents)

RN 353495-59-7 CAPLUS

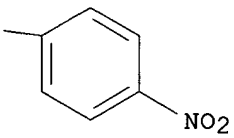
CN 1-Azabicyclo[3.2.0]hept-2-ene-2-carboxylic acid, 3-[[(3S,5S)-5-[[4-[[[bis[[[(4-nitrophenyl)methoxy]carbonyl]amino]methylene]amino]acetyl]hexahydro-1H-1,4-diazepin-1-yl]carbonyl]-1-[[(4-nitrophenyl)methoxy]carbonyl]-3-pyrrolidinyl]thio]-6-[(1R)-1-hydroxyethyl]-4-methyl-7-oxo-, (4-nitrophenyl)methyl ester, (4R,5S,6S)- (9CI) (CA INDEX NAME)

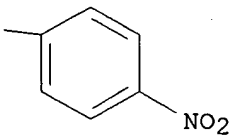
Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



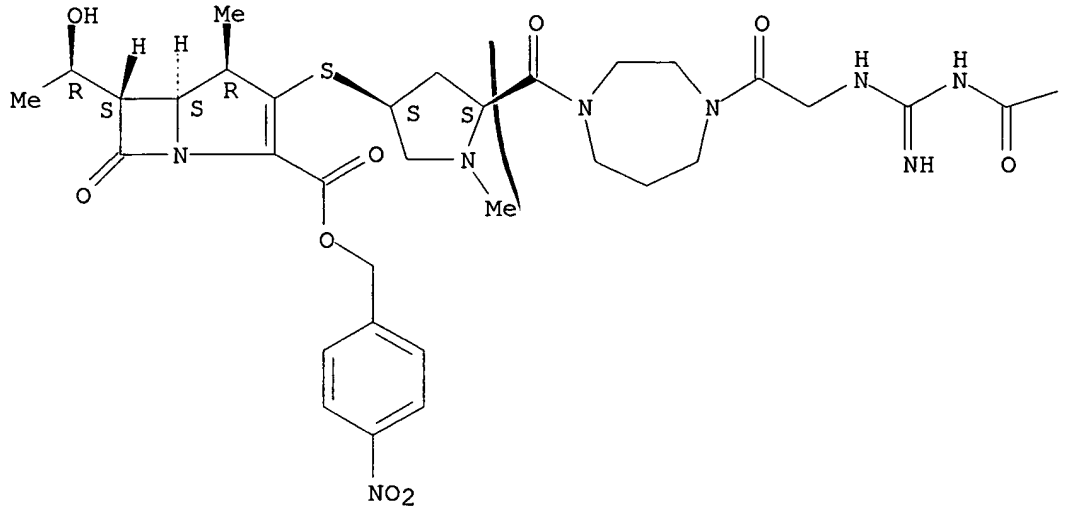


RN 353495-60-0 CAPLUS

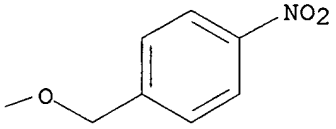
CN 1-Azabicyclo[3.2.0]hept-2-ene-2-carboxylic acid, 3-[[(3S,5S)-5-[[hexahydro-4-[[[imino[[[(4-nitrophenyl)methoxy]carbonyl]amino]methyl]amino]acetyl]-1H-1,4-diazepin-1-yl]carbonyl]-1-methyl-3-pyrrolidinyl]thio]-6-[(1R)-1-hydroxyethyl]-4-methyl-7-oxo-, (4-nitrophenyl)methyl ester, (4R,5S,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



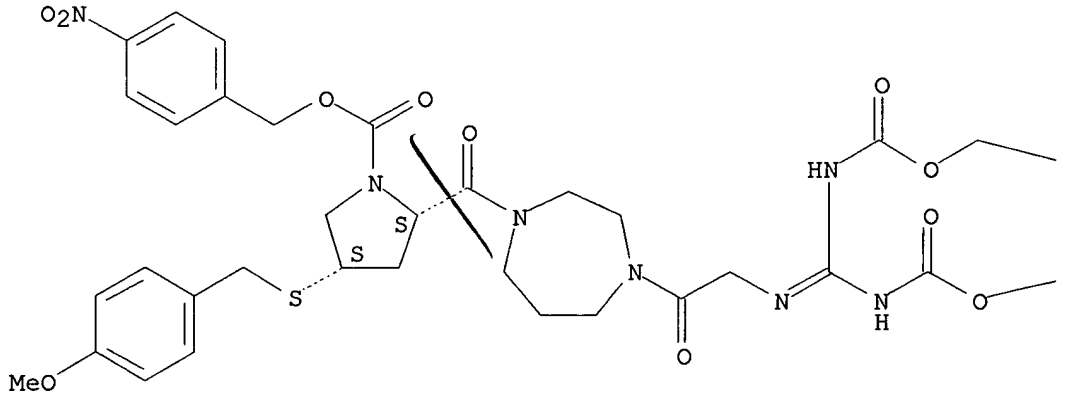
PAGE 1-B

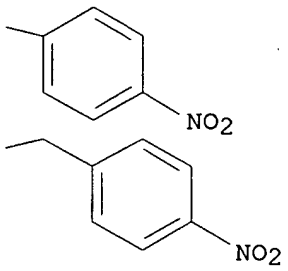


RN 353495-75-7 CAPLUS
CN 1-Pyrrolidinecarboxylic acid, 2-[[4-[[[bis[[[(4-nitrophenyl)methoxy]carbonyl]amino]methylene]amino]acetyl]hexahydro-1H-1,4-diazepin-1-yl]carbonyl]-4-[[(4-methoxyphenyl)methyl]thio]-, (4-nitrophenyl)methyl ester, (2S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A





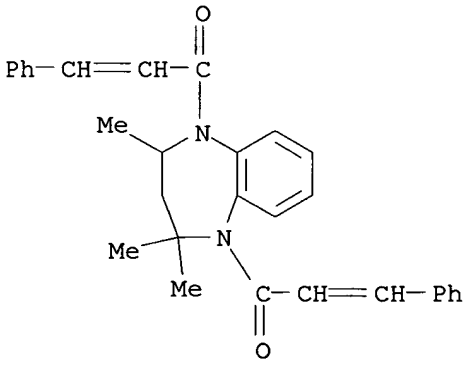
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 14 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:80694 CAPLUS
DOCUMENT NUMBER: 134:260875
TITLE: Synthesis and antiproliferative activity in vitro of novel 1,5-benzodiazepines. Part II
AUTHOR(S): Nawrocka, Wanda; Sztuba, Barbara; Opolski, Adam; Wietrzyk, Joanna; Kowalska, Maria W.; Glowiak, Tadeusz
CORPORATE SOURCE: Department of Technology of Drugs, Wroclaw University of Medicine, Wroclaw, 50-140, Pol.
SOURCE: Archiv der Pharmazie (Weinheim, Germany) (2001), 334(1), 3-10
CODEN: ARPMAS; ISSN: 0365-6233
PUBLISHER: Wiley-VCH Verlag GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 134:260875

AB The reaction of 2,2,4-trimethyl-1H-2,3-dihydro-1,5-benzodiazepine (1) with cinnamoyl chloride leading to the formation of 1-cinnamoyl deriv. 2 is described. Two novel benzodiazepines, 2,2,4-trimethyl-1H-2,3,4,5-tetrahydro-1,5-benzodiazepine (3) and 1-cinnamoyl-2,2,4-trimethyl-1H-2,3,4,5-tetrahydro-1,5-benzodiazepine (4), were synthesized by the redn. of 1 and 2 using NaBH4 in i-PrOH and two other derivs. 5 and 6 were obtained by reaction of 4 with equimolar and dimolar quantity of cinnamoyl chloride, resp. The structures of 1-6 were confirmed by anal. and spectral data (IR, 1H NMR, and MS). 7-Carboxy-2,2,4-trimethyl-1H-2,3-dihydro-1,5-benzodiazepine (7) was synthesized and its crystals were subjected to X-ray anal. Benzodiazepines 1-6 were evaluated for antiproliferative activity in vitro. Three of the compds. tested exhibited cytotoxic activity against human cancer cell lines, namely SW707 (colon cancer), MCF-7 (breast cancer), A549 (lung cancer), and HCV29T (bladder cancer).

IT **332139-96-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis and antiproliferative activity of 1,5-benzodiazepines)

RN 332139-96-5 CAPLUS
CN 1H-1,5-Benzodiazepine, 2,3,4,5-tetrahydro-2,2,4-trimethyl-1,5-bis(1-oxo-3-phenyl-2-propenyl)- (9CI) (CA INDEX NAME)



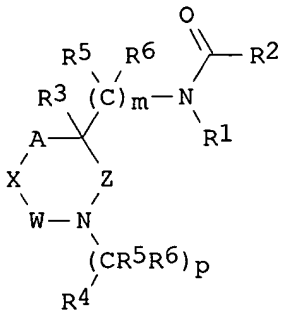
REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 15 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:842113 CAPLUS
DOCUMENT NUMBER: 134:29315
TITLE: Heterocyclic analgesic compounds and methods of use thereof
INVENTOR(S): Cuny, Gregory D.; Shao, Liming; Hauske, James R.; Heffernan, Michele L. R.; Aquila, Brian M.; Wu, Xinhe; Wang, Fengjian; Bannister, Thomas D.
PATENT ASSIGNEE(S): Sepracor, Inc., USA
SOURCE: PCT Int. Appl., 216 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

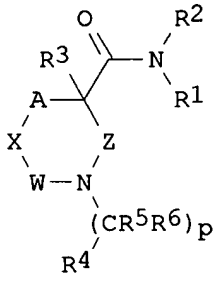
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000071518	A2	20001130	WO 2000-US14579	20000525
WO 2000071518	A3	20011018		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1187810	A2	20020320	EP 2000-937830	20000525
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2003500392	T2	20030107	JP 2000-619775	20000525

PRIORITY APPLN. INFO.:
US 1999-135721P P 19990525
US 1999-168979P P 19991203
US 2000-195809P P 20000411
WO 2000-US14579 W 20000525

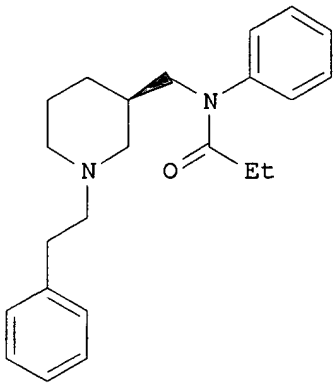
OTHER SOURCE(S): MARPAT 134:29315
GI



I



II



III

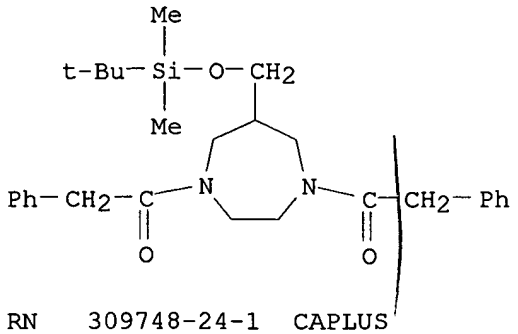
AB The present invention discloses novel nitrogen heterocycles of formula I (A = (CH2)b, Z = (CH2)y, W = (CH2)n, where b = 0 or 1, yr = 1 or 2, and n = 1, 2 or 3 with provisions; X = C(R3)2, O, S, SO2, NR2, NCO2R2, or CO; R1 = alkyl, aryl, heteroaryl, or cycloalkyl; R2 = H, alkyl, fluoroalkyl, aryl, heteroaryl, or cycloalkyl; R1 and R2 may be connected via covalent bond; R3 = H, alkyl, aryl, OR2, OCOR2, CH2OR2, or CO2R2, wherein any two instances of R3 may be connected via divalent carbon bridge; R4 = H, alkyl, aryl, heteroaryl, alkenyl, or cycloalkyl; R5 or R6 = H, alkyl, CH2Y, aryl, heteroaryl, F, OR2 or OCOR2; Y = OR2, N(R2)2, SR2, SOR2, SO2R2 or PO(OR2)2; R4 may be covalently attached to an adjacent R5 or R6; p = 1, 2, 3 or 4; m = 0, 1, or 2) and II (y = 1; n = 2; b = 0) as well as methods for prepn. Compd. III was prepd. by successive amidation of (R)-N-(1-Boc-piperidin-3-ylmethyl)aniline, deprotection and alkylation. Methods employed to prep. claimed compds. included combinatorial chem. providing ninety-six piperidinyl derivs. with IC50 values (.mu.M) ranging 0.31-5.76 and 0.08-4 against .kappa. and .mu. opioid receptors, resp. III was five times stronger [ED50 (.mu.g/kg) <500] than morphine [ED50 <2500] as an analgesic as demonstrated in a std. rat tail flick test. A second aspect of the present invention relates to the use of the novel heterocyclic compds. as ligands for various cellular receptors, including opiate receptors, other the G-protein coupled receptors, and ion channels. An addnl. aspect of the invention relates to the use of the novel heterocyclic compds. as analgesics.

IT **309748-22-9P 309748-24-1P 309748-26-3P 309748-28-5P**

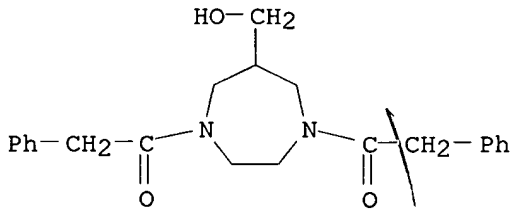
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. and biol. activity of nitrogen heterocyclic analgesic compds.)

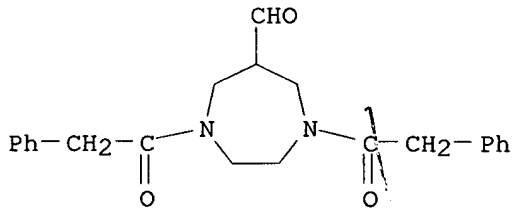
RN 309748-22-9 CAPLUS
CN 1H-1,4-Diazepine, 6-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]hexahydro-1,4-bis(phenylacetyl)- (9CI) (CA INDEX NAME)



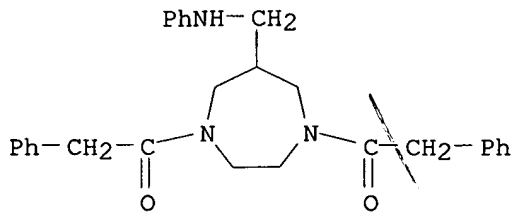
RN 309748-24-1 CAPLUS
CN 1H-1,4-Diazepine-6-methanol, hexahydro-1,4-bis(phenylacetyl)- (9CI) (CA INDEX NAME)



RN 309748-26-3 CAPLUS
CN 1H-1,4-Diazepine-6-carboxaldehyde, hexahydro-1,4-bis(phenylacetyl)- (9CI) (CA INDEX NAME)



RN 309748-28-5 CAPLUS
CN 1H-1,4-Diazepine-6-methanamine, hexahydro-N-phenyl-1,4-bis(phenylacetyl)- (9CI) (CA INDEX NAME)

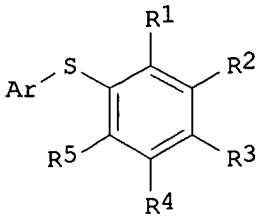


L5 ANSWER 16 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:725609 CAPLUS
DOCUMENT NUMBER: 133:296281
TITLE: Preparation of 2- or 4-(phenylthio)cinnamides as cell adhesion-inhibiting antiinflammatory and immune-suppressive compounds
INVENTOR(S): Link, James; Liu, Gang; Pei, Zhonghua; Von Geldern, Thomas W.; Winn, Martin; Xin, Zhili; Wang, Sheldon; Boyd, Steven A.; Zhu, Gui-Dong; Freeman, Jennifer C.; Gunawardana, Indrani W.; Staeger, Michael A.; Jae, Hwan-soo; Lynch, John K.
PATENT ASSIGNEE(S): Abbott Laboratories, USA
SOURCE: PCT Int. Appl., 476 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000059880	A1	20001012	WO 2000-US8895	20000403
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1165505	A1	20020102	EP 2000-921654	20000403
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 2000009426	A	20020409	BR 2000-9426	20000403
EE 200100513	A	20021216	EE 2001-513	20000403
NO 2001004767	A	20011130	NO 2001-4767	20011001
BG 106029	A	20020531	BG 2001-106029	20011018
HR 2001000776	A1	20021231	HR 2001-776	20011023

PRIORITY APPLN. INFO.:			
US 1999-286645	A	19990402	
US 1999-474517	A	19991229	
US 2000-541795	A	20000331	
WO 2000-US8895	W	20000403	

OTHER SOURCE(S): MARPAT 133:296281
GI



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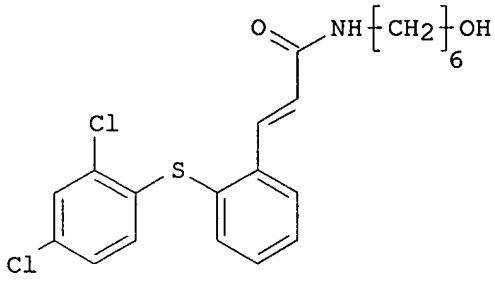


II

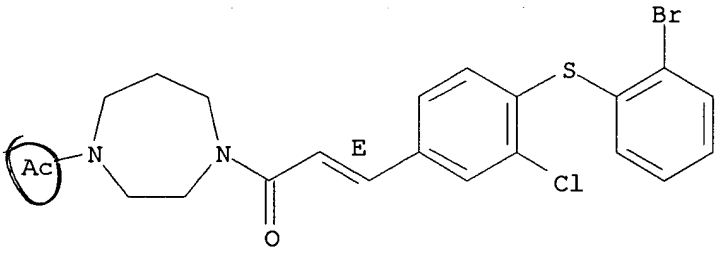
AB The title compds. (I) [wherein R1-R5 = independently H, halo, (halo)alkyl, alkoxy, cyano, NO2, CHO, and least one of R1 or R3 is an (un)substituted cis- or trans-cinnamide; Ar = (un)substituted (hetero)aryl] were prepd. as cell adhesion inhibitors for the treatment of inflammatory and immune diseases. Examples include syntheses for 443 invention compds. and data for 3 bioassays. For instance, a mixt. of 2-[(2,4-dichlorophenyl)thio]benzaldehyde (prepn. given), malonic acid, piperidine in anhyd. pyridine was heated at 110.degree.C for 2 h and then treated with aq. HCl to give trans-2-[(2,4-dichlorophenyl)thio]cinnamic acid (91%). Conversion to the acid chloride followed by amidation with 6-amino-1-hexanol gave (E)-II (90%). In an integrin LFA-1/ICAM-1 biochem. interaction assay, I demonstrated inhibition at 4 .mu.M. In cell-based adhesion assays which measure the ability of test compds. to block adherence of JY-8 cells (a human EBV-transformed B cell line expressing LFA-1 on its surface) to immobilized ICAM-1 or ICAM-3, I exhibited blocking activity at 4 .mu.M and 0.6 .mu.M, resp.

IT **301178-41-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of (phenylthio)cinnamides as cell adhesion inhibitors by coupling of thiophenols with halobenzaldehydes, conversion to cinnamic acids, amidation, and optional derivatization)

RN 301178-41-6 CAPLUS

CN 1H-1,4-Diazepine, 1-acetyl-4-[(2E)-3-[4-[(2-bromophenyl)thio]-3-chlorophenyl]-1-oxo-2-propenyl]hexahydro- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

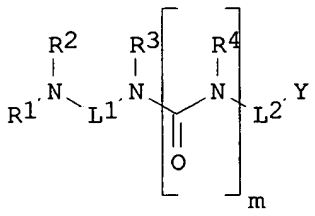
L5 ANSWER 17 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:691093 CAPLUS
DOCUMENT NUMBER: 131:310284
TITLE: Preparation of substituted diamines as .alpha.4.beta.1 mediated cell adhesion inhibitors
INVENTOR(S): Mccarthy, Clive; Harris, Neil Victor; Morley, Andrew David
PATENT ASSIGNEE(S): Rhone-Poulenc Rorer Limited, UK
SOURCE: PCT Int. Appl., 189 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9954321	A1	19991028	WO 1999-GB1230	19990421
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9937164	A1	19991108	AU 1999-37164	19990421

PRIORITY APPLN. INFO.:

GB 1998-8431	A	19980421
GB 1998-11417	A	19980528
US 1998-104139P	P	19981014
US 1998-104238P	P	19981014
WO 1999-GB1230	W	19990421

OTHER SOURCE(S): MARPAT 131:310284
GI



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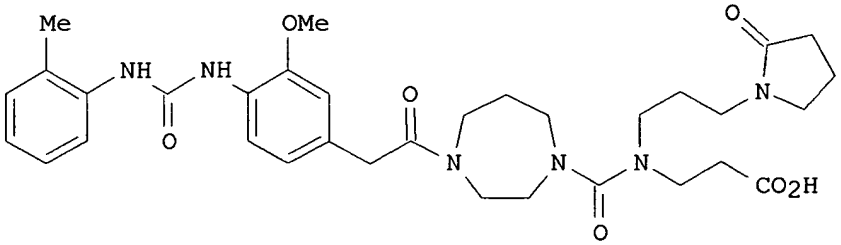


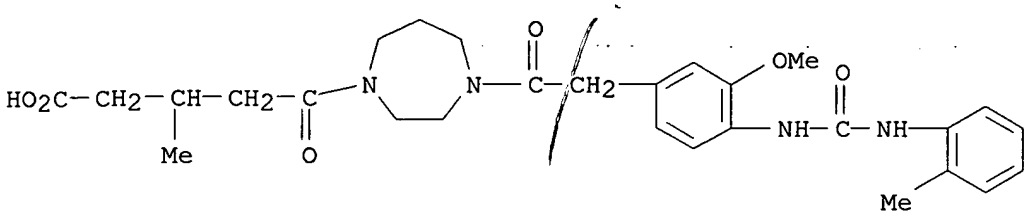
II

AB Substituted diamines (I) [wherein R1 = lower alkyl or various combinations of substituents, such as (cyclo)alkyl, (cyclo)alkenyl, (cyclo)alkynyl, (hetero)aryl(alkyl), etc., and linkage groups, such as C(O), C(S), (un)substituted NHC(O) or NHC(S), S(O), SO2, heteroaryldiyl, heterocycloalkylene, phenylene, etc.; R2 = H or lower alkyl; R3 and R4 = independently H or (un)substituted alkyl, alkenyl, or alkynyl; or R3 and R4 together may = (CH2)n or C(O)CH:CH; L1 = alkylene or (un)substituted (CHR10)pAr(CHR10)p; or L1N(R3) = (un)substituted alkylheterocyclo; or N(R2)L1 = (un)substituted heterocycloalkyl; or N(R2)L1N(R3) = diaza heterocyclo; L2 = (un)substituted alkylene, alkenylene, alkynylene, cycloalkenylene, cycloalkylene, or heterocycloalkylene; Y = carboxy (or an acid bioisostere) or (un)substituted C(O)NH2; Ar = phenylene, (hetero)cycloalkylene, or heteroaryldiyl; R10 = H or lower alkyl; m = 0 or 1; n = 2-4; p = 0-3] were prepd by solid phase synthesis as .alpha.4.beta.1 mediated cell adhesion inhibitors. For example, the ureido deriv. (II) was prepd. using a Wang resin support. The resin was loaded with acryloyl chloride and treated sequentially with 1-(3-aminopropyl)-2-pyrrolidinone, triphosgene, homopiperazine, and 3-methoxy-4-[3-(2-methylphenyl)ureido]phenylacetic acid to yield II. Compds. of formula I regulate the interaction of VCAM-1 and fibronectin with the integrin VLA-4 (.alpha.4.beta.1). Particular compds. of the invention suppressed cell adhesion to fibronectin and VCAM-1 with IC50 values ranging from 100.mu.M to 1 nM in assays on metabolically labeled RAMOS cells. Particular compds. also inhibited airway inflammation after antigen challenge in mice and rats. The inhibitors caused a statistically significant redn. in eosinophil and lymphocyte nos. in bronchoalveolar lavage (BAL) and airway tissue. The invention compds., their prodrugs, pharmaceutically acceptable salts, and solvates, are useful for the treatment of inflammatory diseases and asthma.

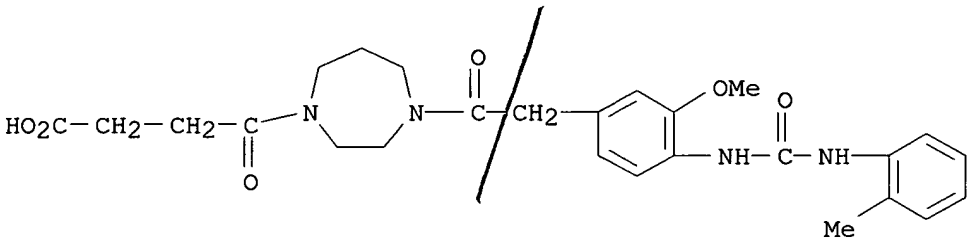
IT **247253-93-6P 247253-94-7P 247253-95-8P**
247253-96-9P 247253-97-0P 247253-98-1P
247253-99-2P 247254-00-8P 247254-01-9P
247254-02-0P 247254-03-1P 247254-04-2P
247254-05-3P 247254-07-5P 247254-08-6P
247254-09-7P 247254-10-0P 247254-11-1P
247254-12-2P 247254-13-3P 247254-14-4P
247254-15-5P 247254-16-6P 247254-17-7P
247254-18-8P 247254-19-9P 247254-20-2P
247254-21-3P 247254-22-4P 247254-23-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(target compd.; prepn. of substituted diamines as .alpha.4.beta.1 mediated cell adhesion inhibitors for treatment of inflammatory diseases and asthma)

RN 247253-93-6 CAPLUS

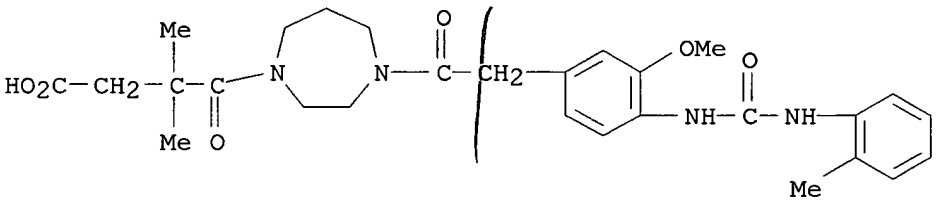
CN 1H-1,4-Diazepine-1-pentanoic acid, hexahydro-4-[[3-methoxy-4-[[[(2-methylphenyl)amino]carbonyl]amino]phenyl]acetyl]-.beta.-methyl-.delta.-oxo- (9CI) (CA INDEX NAME)



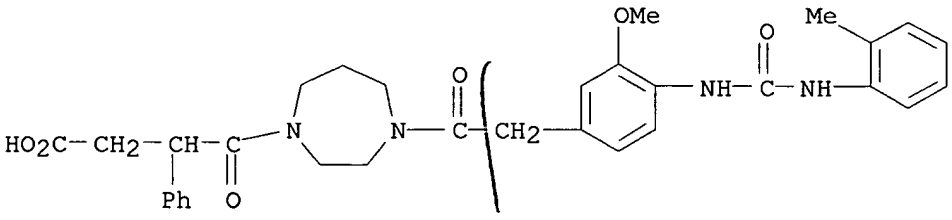
RN 247253-94-7 CAPLUS
CN 1H-1,4-Diazepine-1-butanoic acid, hexahydro-4-[[3-methoxy-4-[[[(2-methylphenyl)amino]carbonyl]amino]phenyl]acetyl]-.gamma.-oxo- (9CI) (CA INDEX NAME)



RN 247253-95-8 CAPLUS
CN 1H-1,4-Diazepine-1-butanoic acid, hexahydro-4-[[3-methoxy-4-[[[(2-methylphenyl)amino]carbonyl]amino]phenyl]acetyl]-.beta.,.beta.-dimethyl-.gamma.-oxo- (9CI) (CA INDEX NAME)

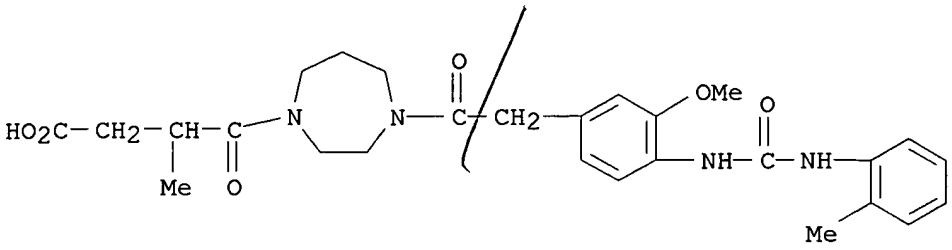


RN 247253-96-9 CAPLUS
CN 1H-1,4-Diazepine-1-butanoic acid, hexahydro-4-[[3-methoxy-4-[[[(2-methylphenyl)amino]carbonyl]amino]phenyl]acetyl]-.gamma.-oxo-.beta.-phenyl- (9CI) (CA INDEX NAME)

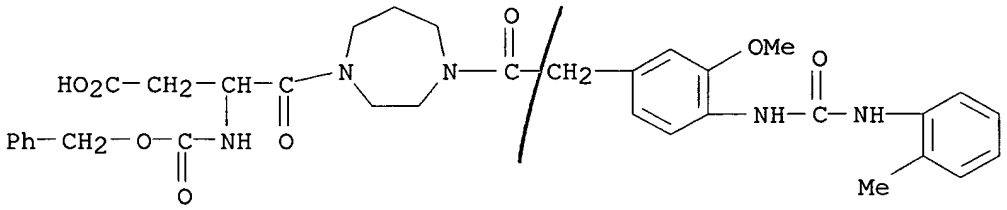


RN 247253-97-0 CAPLUS
CN 1H-1,4-Diazepine-1-butanoic acid, hexahydro-4-[[3-methoxy-4-[[[(2-methylphenyl)amino]carbonyl]amino]phenyl]acetyl]-.beta.-methyl-.gamma.-oxo-

(9CI) (CA INDEX NAME)

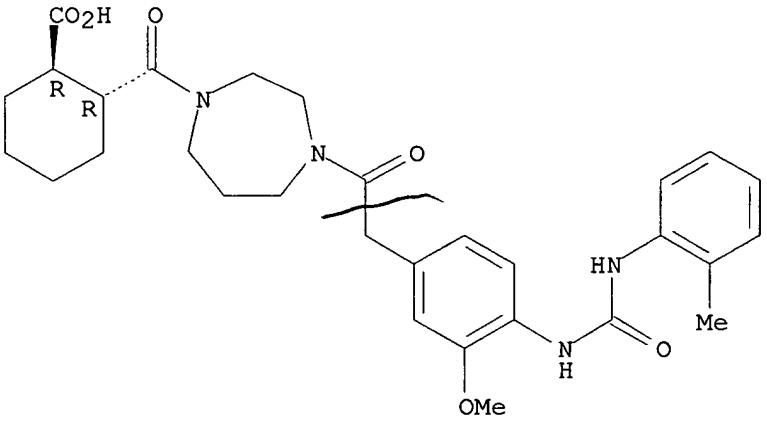


RN 247253-98-1 CAPLUS
CN 1H-1,4-Diazepine-1-butanoic acid, hexahydro-4-[[3-methoxy-4-[[[(2-methylphenyl)amino]carbonyl]amino]phenyl]acetyl]-.gamma.-oxo-.beta.-[[(phenylmethoxy)carbonyl]amino]- (9CI) (CA INDEX NAME)

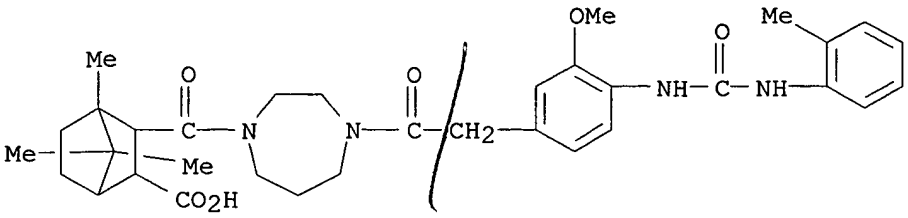


RN 247253-99-2 CAPLUS
CN Cyclohexanecarboxylic acid, 2-[[hexahydro-4-[[3-methoxy-4-[[[(2-methylphenyl)amino]carbonyl]amino]phenyl]acetyl]-1H-1,4-diazepin-1-yl]carbonyl]-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

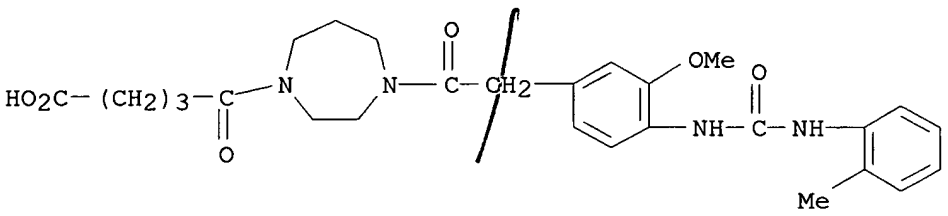
Relative stereochemistry.



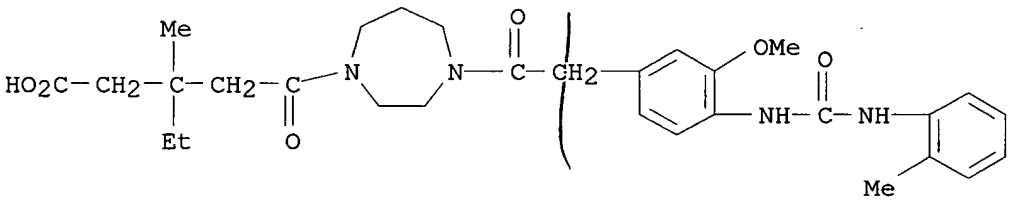
RN 247254-00-8 CAPLUS
CN Bicyclo[2.2.1]heptane-2-carboxylic acid, 3-[[hexahydro-4-[[3-methoxy-4-[[[(2-methylphenyl)amino]carbonyl]amino]phenyl]acetyl]-1H-1,4-diazepin-1-yl]carbonyl]-4,7,7-trimethyl- (9CI) (CA INDEX NAME)



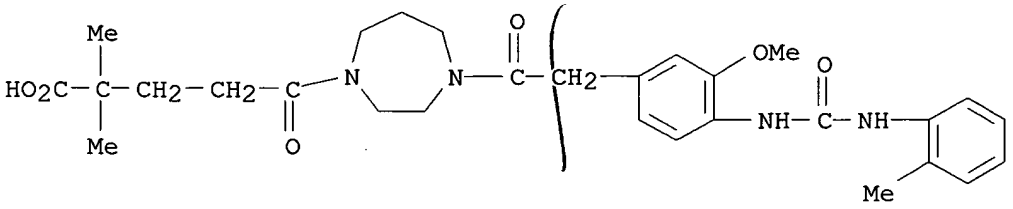
RN 247254-01-9 CAPLUS
CN 1H-1,4-Diazepine-1-pentanoic acid, hexahydro-4-[[3-methoxy-4-[[[(2-methylphenyl)amino]carbonyl]amino]phenyl]acetyl]-.delta.-oxo- (9CI) (CA INDEX NAME)



RN 247254-02-0 CAPLUS
CN 1H-1,4-Diazepine-1-pentanoic acid, .beta.-ethylhexahydro-4-[[3-methoxy-4-[[[(2-methylphenyl)amino]carbonyl]amino]phenyl]acetyl]-.beta.-methyl-.delta.-oxo- (9CI) (CA INDEX NAME)



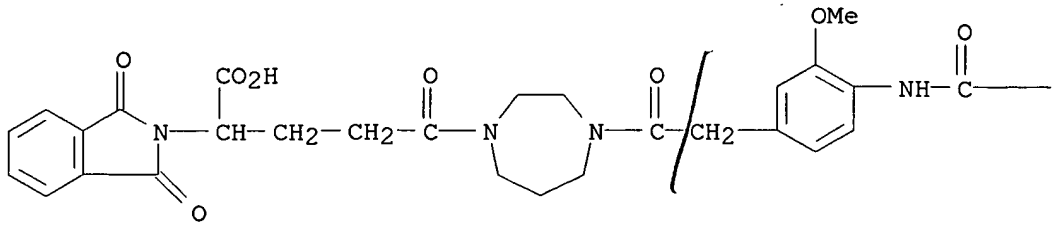
RN 247254-03-1 CAPLUS
CN 1H-1,4-Diazepine-1-pentanoic acid, hexahydro-4-[[3-methoxy-4-[[[(2-methylphenyl)amino]carbonyl]amino]phenyl]acetyl]-.alpha.,.alpha.-dimethyl-.delta.-oxo- (9CI) (CA INDEX NAME)



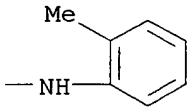
RN 247254-04-2 CAPLUS
CN 2H-Isoindole-2-acetic acid, .alpha.-[3-[hexahydro-4-[[3-methoxy-4-[[[(2-

methylphenyl)amino]carbonyl]amino]phenyl]acetyl]-1H-1,4-diazepin-1-yl]-3-oxopropyl]-1,3-dihydro-1,3-dioxo- (9CI) (CA INDEX NAME)

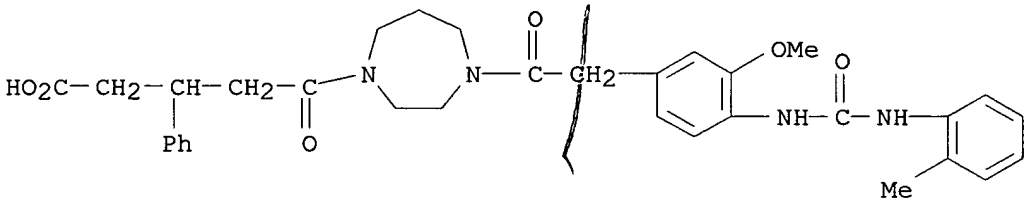
PAGE 1-A



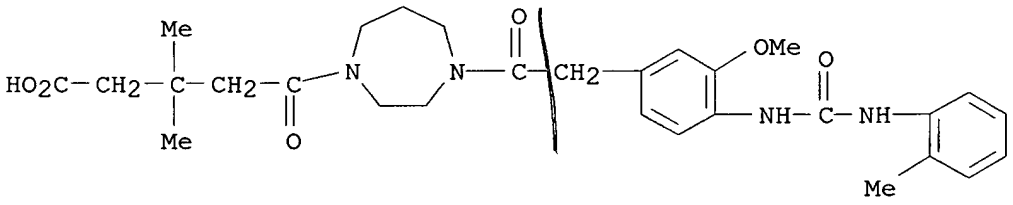
PAGE 1-B



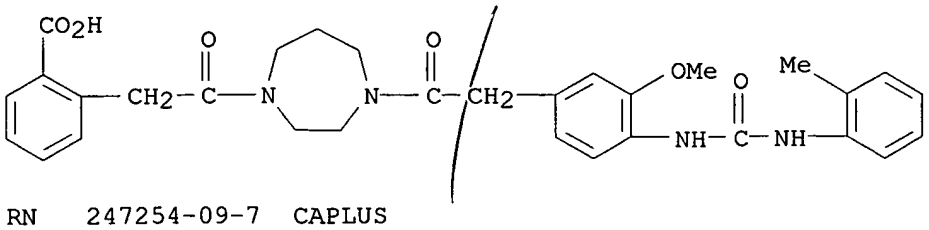
RN 247254-05-3 CAPLUS
CN 1H-1,4-Diazepine-1-pentanoic acid, hexahydro-4-[[3-methoxy-4-[[[(2-methylphenyl)amino]carbonyl]amino]phenyl]acetyl]-.delta.-oxo-.beta.-phenyl- (9CI) (CA INDEX NAME)



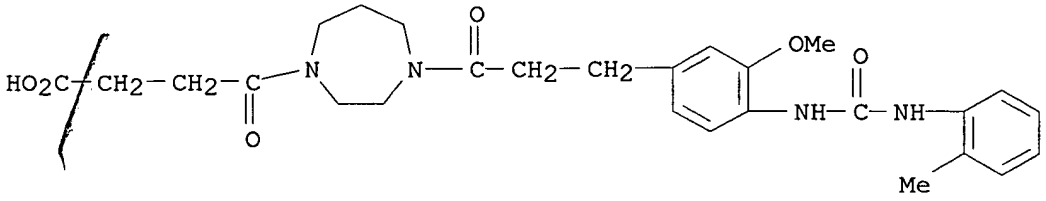
RN 247254-07-5 CAPLUS
CN 1H-1,4-Diazepine-1-pentanoic acid, hexahydro-4-[[3-methoxy-4-[[[(2-methylphenyl)amino]carbonyl]amino]phenyl]acetyl]-.beta.,.beta.-dimethyl-.delta.-oxo- (9CI) (CA INDEX NAME)



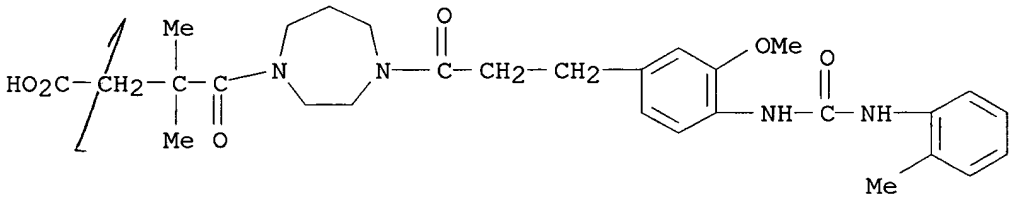
RN 247254-08-6 CAPLUS
CN Benzoic acid, 2-[2-[hexahydro-4-[[3-methoxy-4-[[[(2-methylphenyl)amino]carbonyl]amino]phenyl]acetyl]-1H-1,4-diazepin-1-yl]-2-oxoethyl]- (9CI) (CA INDEX NAME)



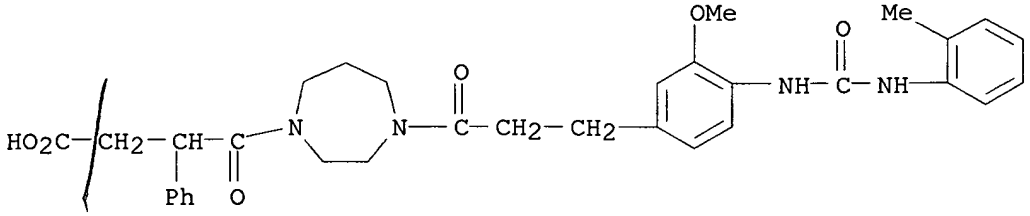
RN 247254-09-7 CAPLUS
CN 1H-1,4-Diazepine-1-butanoic acid, hexahydro-4-[3-[3-methoxy-4-[[[(2-methylphenyl)amino]carbonyl]amino]phenyl]-1-oxopropyl]-.gamma.-oxo- (9CI) (CA INDEX NAME)



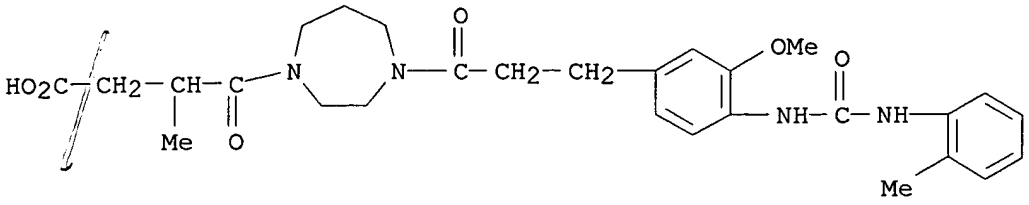
RN 247254-10-0 CAPLUS
CN 1H-1,4-Diazepine-1-butanoic acid, hexahydro-4-[3-[3-methoxy-4-[[[(2-methylphenyl)amino]carbonyl]amino]phenyl]-1-oxopropyl]-.beta.,.beta.-dimethyl-.gamma.-oxo- (9CI) (CA INDEX NAME)



RN 247254-11-1 CAPLUS
CN 1H-1,4-Diazepine-1-butanoic acid, hexahydro-4-[3-[3-methoxy-4-[[[(2-methylphenyl)amino]carbonyl]amino]phenyl]-1-oxopropyl]-.gamma.-oxo-.beta.-phenyl- (9CI) (CA INDEX NAME)

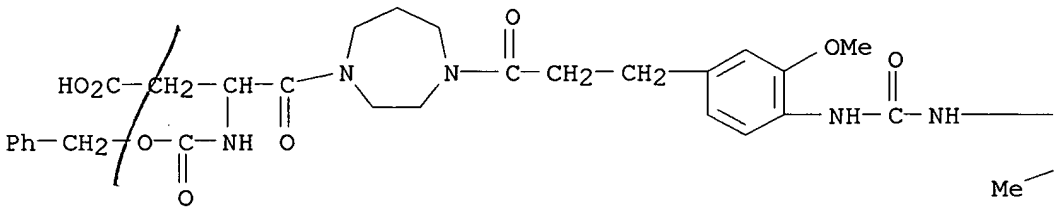


RN 247254-12-2 CAPLUS
CN 1H-1,4-Diazepine-1-butanoic acid, hexahydro-4-[3-[3-methoxy-4-[[[(2-methylphenyl)amino]carbonyl]amino]phenyl]-1-oxopropyl]-.beta.-methyl-.gamma.-oxo- (9CI) (CA INDEX NAME)



RN 247254-13-3 CAPLUS
CN 1H-1,4-Diazepine-1-butanoic acid, hexahydro-4-[3-[3-methoxy-4-[[[(2-methylphenyl)amino]carbonyl]amino]phenyl]-1-oxopropyl]-.gamma.-oxo-.beta.-[[(phenylmethoxy)carbonyl]amino]- (9CI) (CA INDEX NAME)

PAGE 1-A



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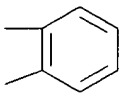
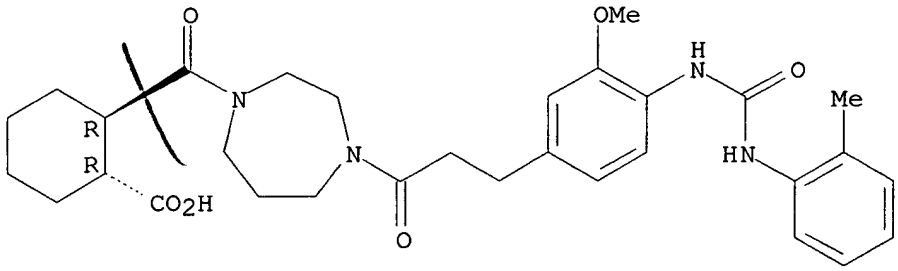


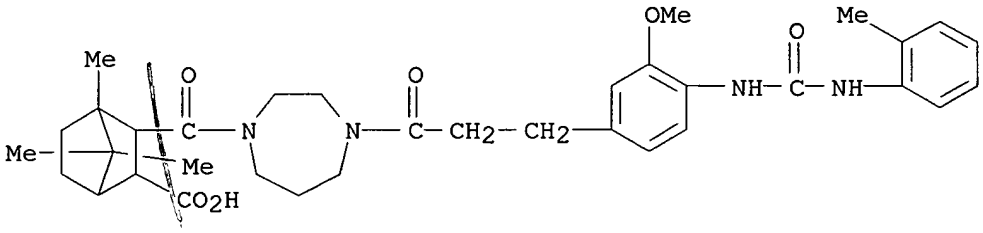
RN 247254-14-4 CAPLUS
CN Cyclohexanecarboxylic acid, 2-[[hexahydro-4-[3-[3-methoxy-4-[[[(2-methylphenyl)amino]carbonyl]amino]phenyl]-1-oxopropyl]-1H-1,4-diazepin-1-yl]carbonyl]-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

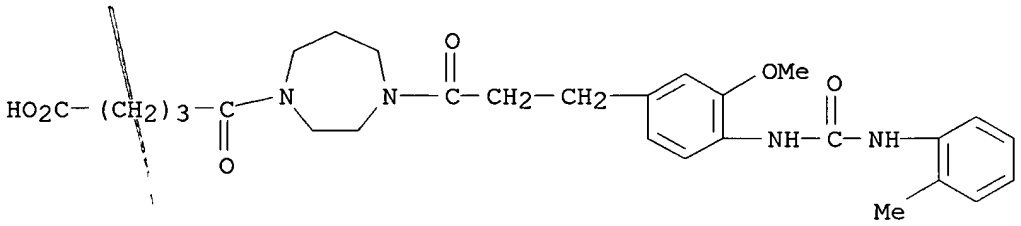


RN 247254-15-5 CAPLUS

CN Bicyclo[2.2.1]heptane-2-carboxylic acid, 3-[[hexahydro-4-[3-[3-methoxy-4-[[[(2-methylphenyl)amino]carbonyl]amino]phenyl]-1-oxopropyl]-1H-1,4-diazepin-1-yl]carbonyl]-4,7,7-trimethyl- (9CI) (CA INDEX NAME)

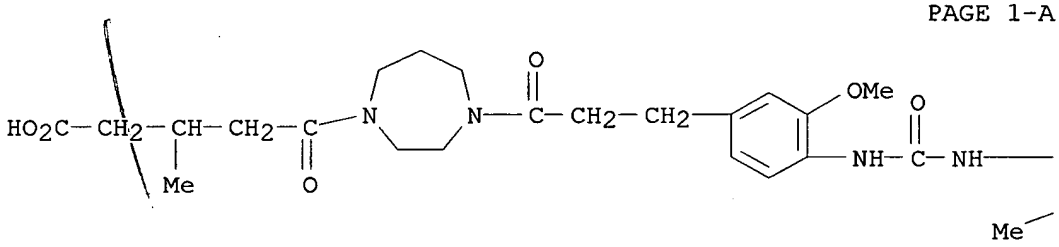


RN 247254-16-6 CAPLUS
CN 1H-1,4-Diazepine-1-pentanoic acid, hexahydro-4-[3-[3-methoxy-4-[[[(2-methylphenyl)amino]carbonyl]amino]phenyl]-1-oxopropyl]-.delta.-oxo- (9CI) (CA INDEX NAME)



RN 247254-17-7 CAPLUS
CN 1H-1,4-Diazepine-1-pentanoic acid, hexahydro-4-[3-[3-methoxy-4-[[[(2-methylphenyl)amino]carbonyl]amino]phenyl]-1-oxopropyl]-.beta.-methyl-.delta.-oxo- (9CI) (CA INDEX NAME)

PAGE 1-A



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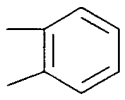
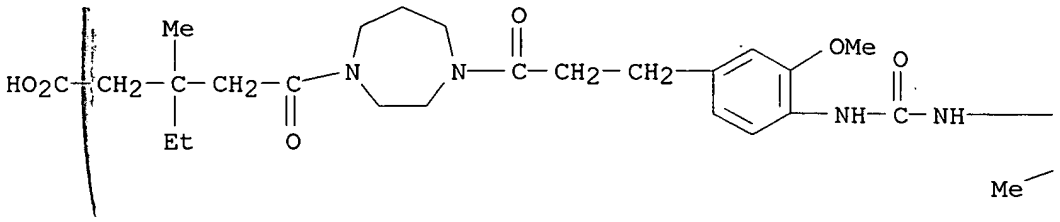


RN 247254-18-8 CAPLUS
CN 1H-1,4-Diazepine-1-pentanoic acid, .beta.-ethylhexahydro-4-[3-[3-methoxy-4-[[[(2-methylphenyl)amino]carbonyl]amino]phenyl]-1-oxopropyl]-.beta.-methyl-.delta.-oxo- (9CI) (CA INDEX NAME)

PAGE 1-A



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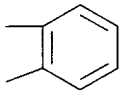

RN 247254-19-9 CAPLUS
CN 1H-1,4-Diazepine-1-pentanoic acid, hexahydro-4-[3-[3-methoxy-4-[[[(2-methylphenyl)amino]carbonyl]amino]phenyl]-1-oxopropyl]-.alpha.,.alpha.-dimethyl-.delta.-oxo- (9CI) (CA INDEX NAME)

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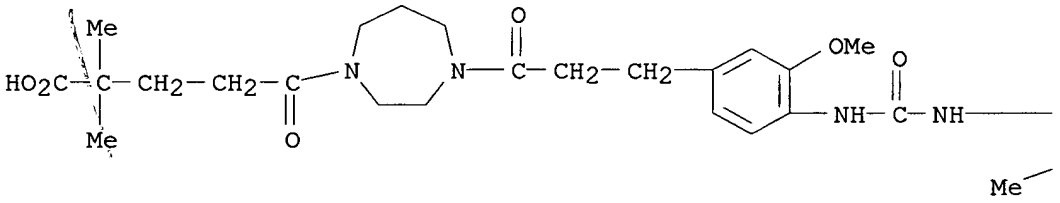

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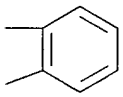
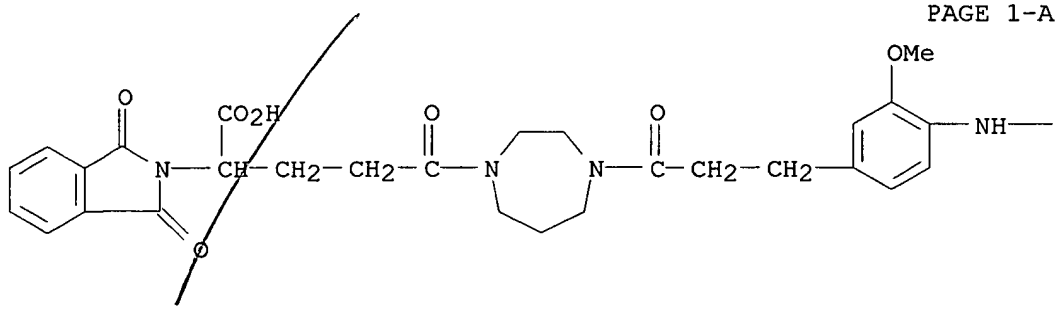


RN 247254-20-2 CAPLUS
CN 2H-Isoindole-2-acetic acid, .alpha.-[3-[hexahydro-4-[3-[3-methoxy-4-[[[(2-

methylphenyl)amino]carbonyl]amino]phenyl]-1-oxopropyl]-1H-1,4-diazepin-1-yl]-3-oxopropyl]-1,3-dihydro-1,3-dioxo- (9CI) (CA INDEX NAME)

PAGE 1-A



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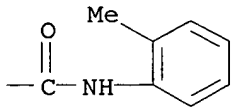
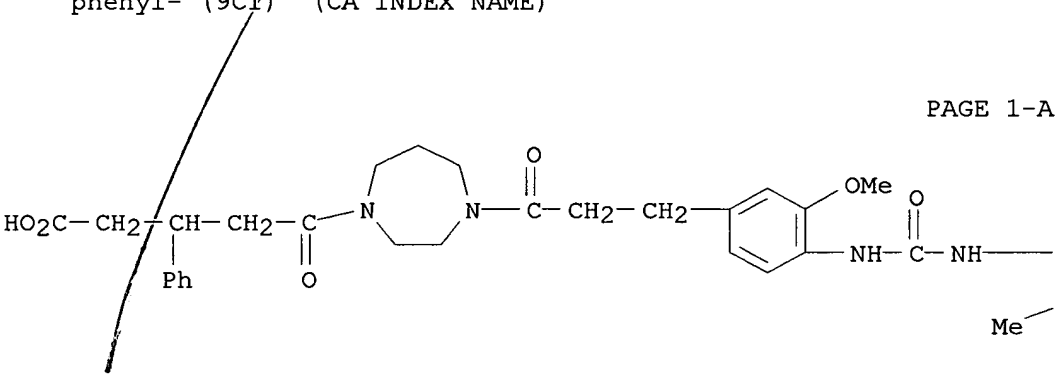


RN 247254-21-3 CAPLUS
CN 1H-1,4-Diazepine-1-pentanoic acid, hexahydro-4-[3-[3-methoxy-4-[[[(2-methylphenyl)amino]carbonyl]amino]phenyl]-1-oxopropyl]-.delta.-oxo-.beta.-phenyl- (9CI) (CA INDEX NAME)

PAGE 1-A



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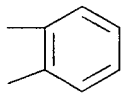

RN 247254-22-4 CAPLUS
CN 1H-1,4-Diazepine-1-pentanoic acid, hexahydro-4-[3-[3-methoxy-4-[[[(2-methylphenyl)amino]carbonyl]amino]phenyl]-1-oxopropyl]-.beta.,.beta.-dimethyl-.delta.-oxo- (9CI) (CA INDEX NAME)

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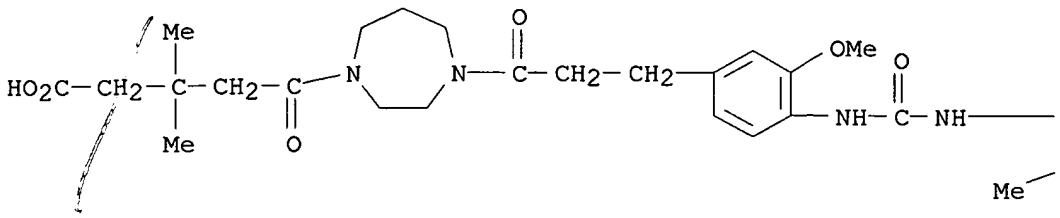

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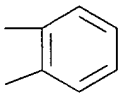
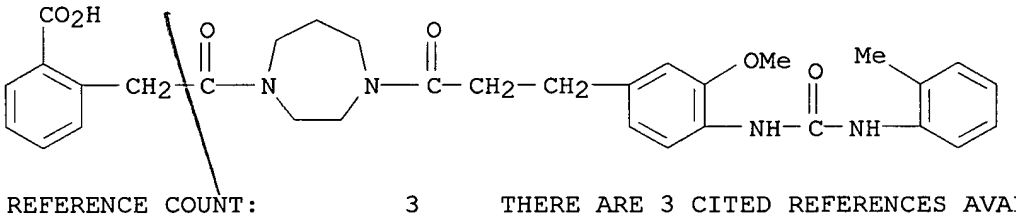


RN 247254-23-5 CAPLUS
CN Benzoic acid, 2-[2-[hexahydro-4-[3-[3-methoxy-4-[[[(2-methylphenyl)amino]carbonyl]amino]phenyl]-1-oxopropyl]-1H-1,4-diazepin-1-yl]-2-oxoethyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 18 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:156359 CAPLUS
DOCUMENT NUMBER: 130:209726
TITLE: 7-Phenyl-1,4-diazepines as neurokinin receptor antagonists
INVENTOR(S): David, Samuel; Antel, Jochen; Bruckner, Reinhard; Ziegler, Dieter; Eeckout, Christian; Bielenberg, Gerhard-Wilhelm; Peck, Michael
PATENT ASSIGNEE(S): Solvay Pharmaceuticals G.m.b.H., Germany
SOURCE: Eur. Pat. Appl., 45 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 899264	A1	19990303	EP 1998-115651	19980820
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
DE 19737334	A1	19990304	DE 1997-19737334	19970827
ZA 9806719	A	19990202	ZA 1998-6719	19980728
JP 11116557	A2	19990427	JP 1998-237129	19980824
NZ 331523	A	20000228	NZ 1998-331523	19980824
CA 2245926	AA	19990227	CA 1998-2245926	19980826
NO 9803919	A	19990301	NO 1998-3919	19980826
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CN 1220262	A	19990623	CN 1998-118497	19980827
BR 9803250	A	20000208	BR 1998-3250	19980827
US 6040303	A	20000321	US 1998-141312	19980827

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OTHER SOURCE(S): MARPAT 130:209726
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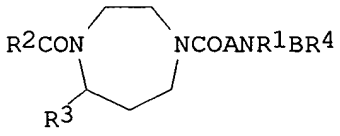

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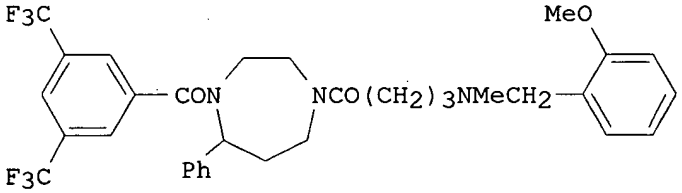


II

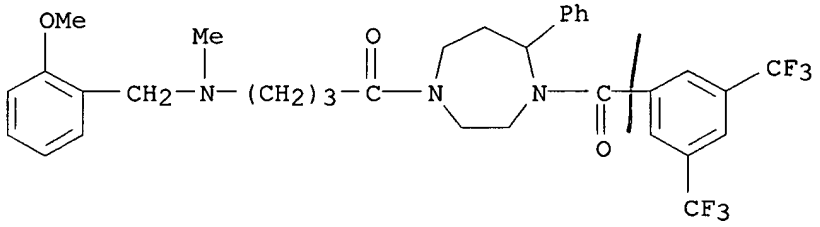
AB Title compds. I [R1 = H, alkyl; R2-R4 = (un)substituted Ph; A = (CH2)n, NH(CH2)m; n = 1-3; m = 2, 3; B = alkylene] were prepd. Thus, the

diazepine II was prepd. from 4-aminobutyric acid, 2-methoxybenzaldehyde, and Et benzoylacetate in 6 steps. II had a Ki for in vitro binding to the NK-1 receptor of 0.012 .mu.M/L.

IT **220896-75-3P 220896-76-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of phenylperhydrodiazepines as neurokinin receptor antagonists)

RN 220896-75-3 CAPLUS

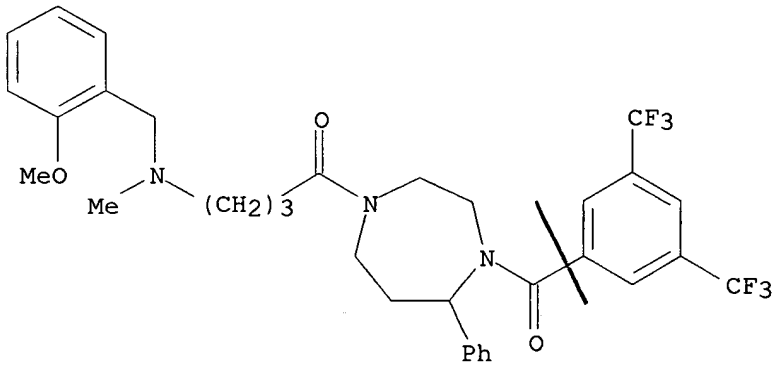
CN 1H-1,4-Diazepine, 4-[3,5-bis(trifluoromethyl)benzoyl]hexahydro-1-[4-[[(2-methoxyphenyl)methyl]methylamino]-1-oxobutyl]-5-phenyl- (9CI) (CA INDEX NAME)



RN 220896-76-4 CAPLUS

CN 1H-1,4-Diazepine, 4-[3,5-bis(trifluoromethyl)benzoyl]hexahydro-1-[4-[[(2-methoxyphenyl)methyl]methylamino]-1-oxobutyl]-5-phenyl-, (-)- (9CI) (CA INDEX NAME)

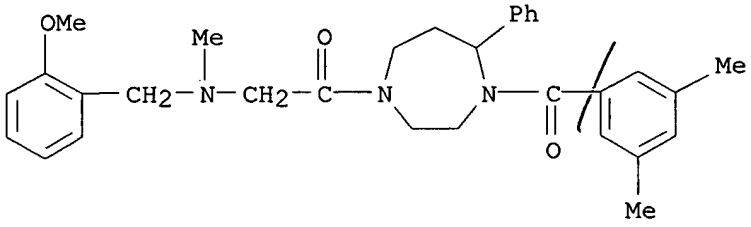
Rotation (-).



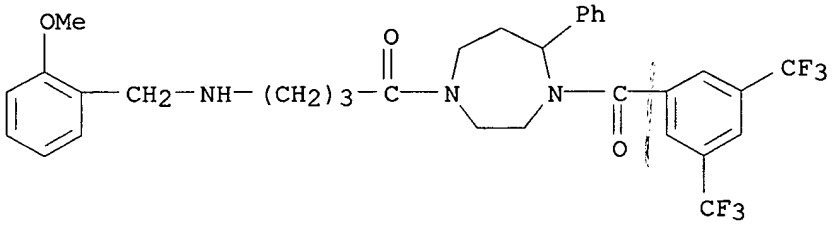
IT **220896-78-6P 220896-91-3P 220897-01-8P 220897-05-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of phenylperhydrodiazepines as neurokinin receptor antagonists)

RN 220896-78-6 CAPLUS

CN 1H-1,4-Diazepine, 4-(3,5-dimethylbenzoyl)hexahydro-1-[[[(2-methoxyphenyl)methyl]methylamino]acetyl]-5-phenyl- (9CI) (CA INDEX NAME)



RN 220896-91-3 CAPLUS
CN 1H-1,4-Diazepine, 4-[3,5-bis(trifluoromethyl)benzoyl]hexahydro-1-[4-[[(2-methoxyphenyl)methyl]amino]-1-oxobutyl]-5-phenyl- (9CI) (CA INDEX NAME)



RN 220897-01-8 CAPLUS
CN 1H-1,4-Diazepine, 4-[3,5-bis(trifluoromethyl)benzoyl]hexahydro-1-[4-[[(2-methoxyphenyl)methyl]methylamino]-1-oxobutyl]-5-phenyl-, monohydrochloride (9CI) (CA INDEX NAME)

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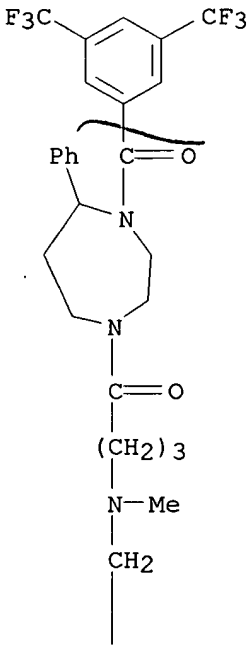

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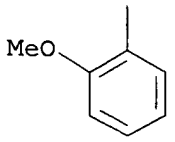
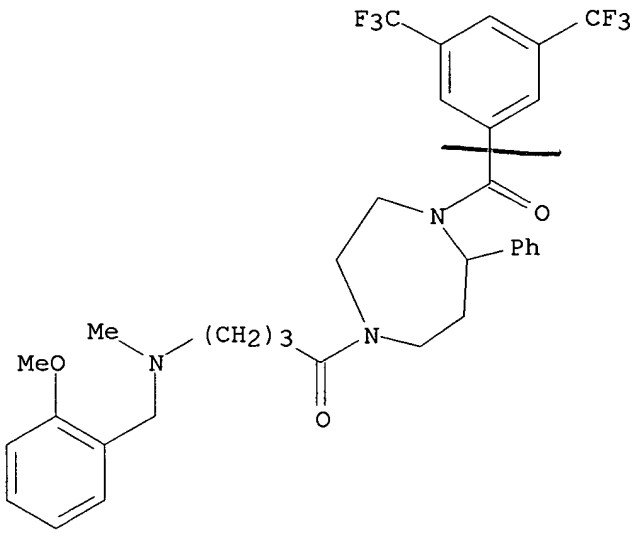


● HCl

RN 220897-05-2 CAPLUS
CN 1H-1,4-Diazepine, 4-[3,5-bis(trifluoromethyl)benzoyl]hexahydro-1-[4-[[(2-methoxyphenyl)methyl]methylamino]-1-oxobutyl]-5-phenyl-, monohydrochloride, (-)- (9CI) (CA INDEX NAME)

Rotation (-).



● HCl

IT **220896-77-5P 220896-85-5P 220896-86-6P**
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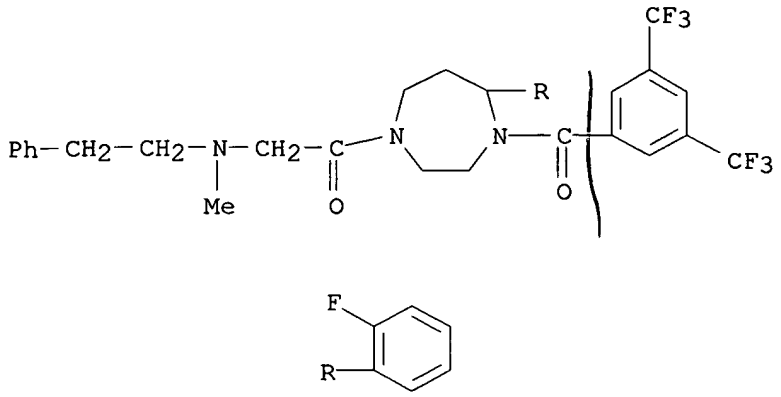
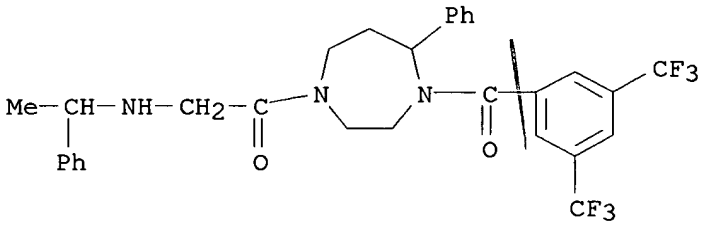
220896-93-5P 220896-94-6P 220896-95-7P
220896-97-9P 220896-98-0P 220897-54-1P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of phenylperhydrodiazepines as neurokinin receptor antagonists)
RN 220896-77-5 CAPLUS
CN 1H-1,4-Diazepine, 4-[3,5-bis(trifluoromethyl)benzoyl]-5-(2-fluorophenyl)hexahydro-1-[[methyl(2-phenylethyl)amino]acetyl]- (9CI) (CA INDEX NAME)



RN 220896-85-5 CAPLUS
CN 1H-1,4-Diazepine, 4-[3,5-bis(trifluoromethyl)benzoyl]hexahydro-5-phenyl-1-[[(1-phenylethyl)amino]acetyl]- (9CI) (CA INDEX NAME)



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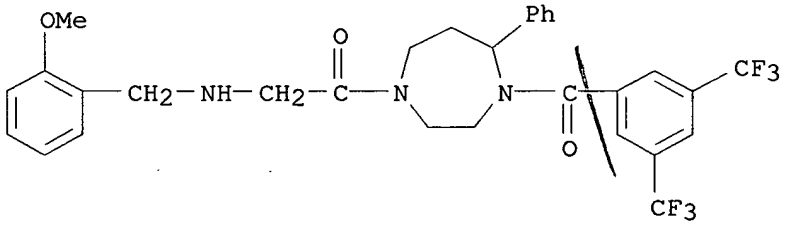
CN 1H-1,4-Diazepine, 4-[3,5-bis(trifluoromethyl)benzoyl]hexahydro-1-[[[(2-methoxyphenyl)methyl]amino]acetyl]-5-phenyl- (9CI) (CA INDEX NAME)



RN 220896-87-7 CAPLUS
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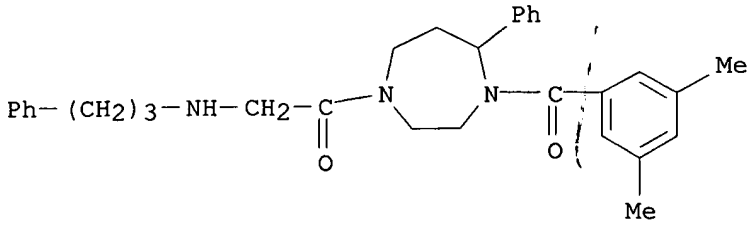

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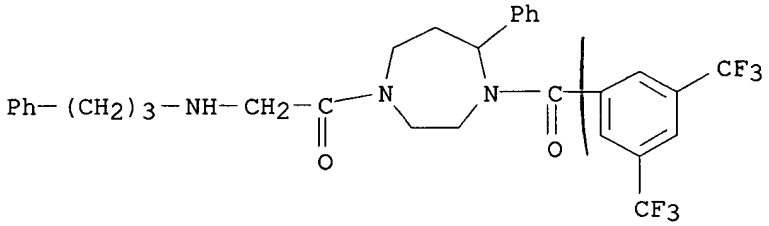

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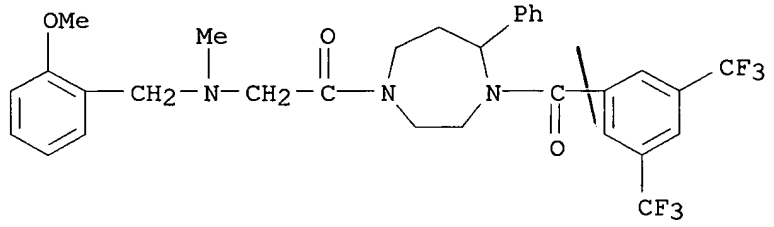

RN 220896-93-5 CAPLUS
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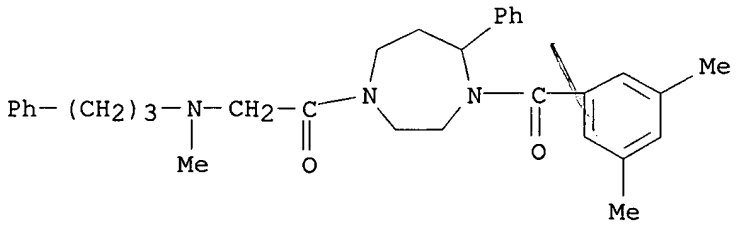

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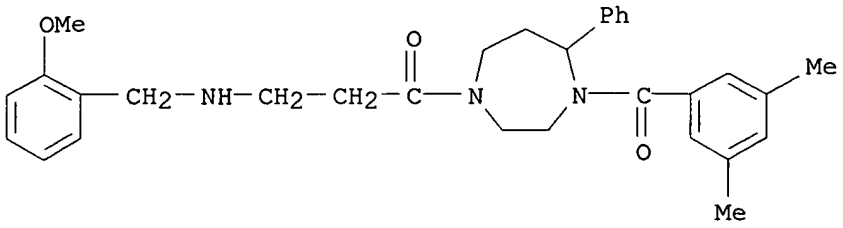
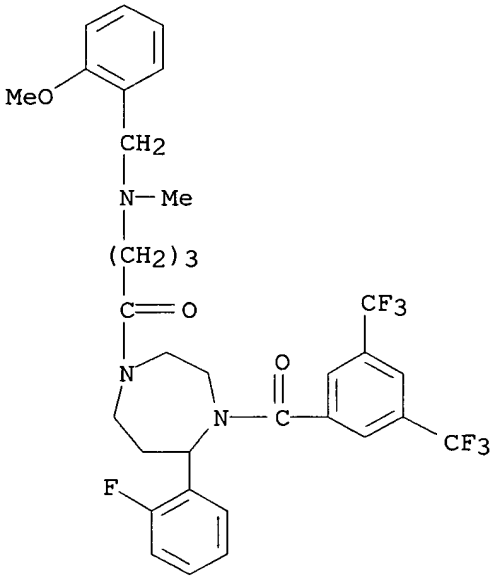
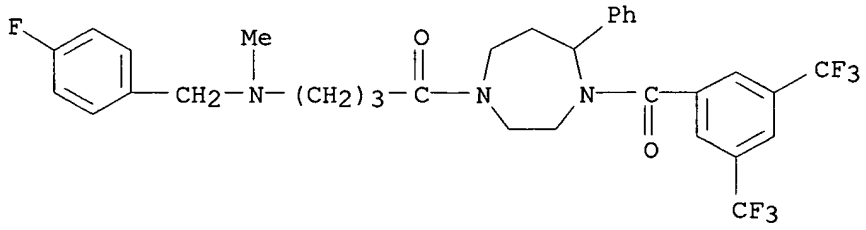


RN 220896-95-7 CAPLUS
CN 1H-1,4-Diazepine, 4-[3,5-bis(trifluoromethyl)benzoyl]-5-(2-fluorophenyl)hexahydro-1-[4-[[(2-methoxyphenyl)methyl]methylamino]-1-oxobutyl]- (9CI) (CA INDEX NAME)

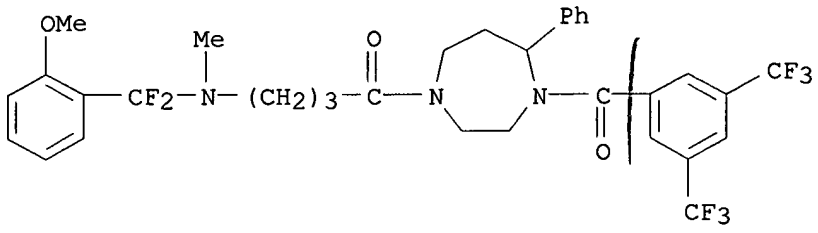


RN 220896-97-9 CAPLUS
CN 1H-1,4-Diazepine, 4-[3,5-bis(trifluoromethyl)benzoyl]-1-[4-[[(4-fluorophenyl)methyl]methylamino]-1-oxobutyl]hexahydro-5-phenyl- (9CI) (CA INDEX NAME)



RN 220896-98-0 CAPLUS

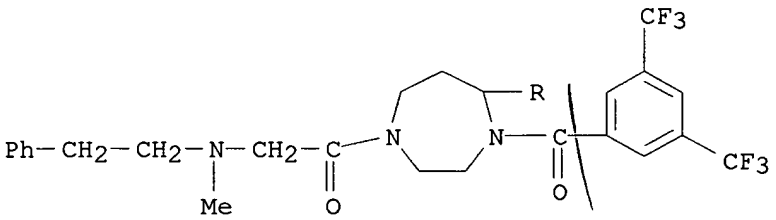
CN 1H-1,4-Diazepine, 4-[3,5-bis(trifluoromethyl)benzoyl]-1-[4-[[difluoro(2-methoxyphenyl)methyl]methylamino]-1-oxobutyl]hexahydro-5-phenyl- (9CI) (CA INDEX NAME)

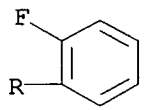


RN 220897-54-1 CAPLUS
CN 1H-1,4-Diazepine, 4-[3,5-bis(trifluoromethyl)benzoyl]-5-(2-fluorophenyl)hexahydro-1-[[methyl(2-phenylethyl)amino]acetyl]-, (2Z)-2-butenedioate (9CI) (CA INDEX NAME)

CM 1

CRN 220896-77-5
CMF C31 H30 F7 N3 O2

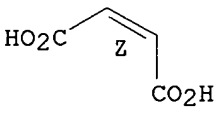




CM 2

CRN 110-16-7
CMF C4 H4 O4

Double bond geometry as shown.



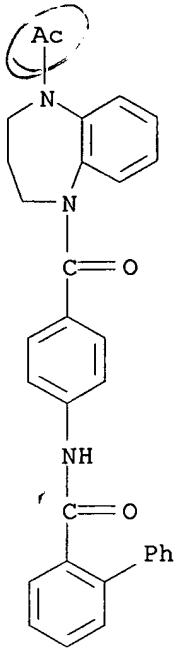
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 19 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1998:700652 CAPLUS
DOCUMENT NUMBER: 130:52394
TITLE: Nonpeptide arginine vasopressin antagonists for both V1A and V2 receptors: synthesis and pharmacological properties of 2-phenyl-4'-(2,3,4,5-tetrahydro-1H-1,5-benzodiazepine-1-carbonyl)benzanilide derivatives
AUTHOR(S): Matsuhisa, Akira; Koshio, Hiroyuki; Sakamoto, Kenichiro; Taniguchi, Nobuaki; Yatsu, Takeyuki; Tanaka, Akihiro
CORPORATE SOURCE: Institute for Drug Discovery Research, Yamanouchi Pharmaceutical Co., Ltd., Tsukuba, 305-8585, Japan
SOURCE: Chemical & Pharmaceutical Bulletin (1998), 46(10), 1566-1579
CODEN: CPBTAL; ISSN: 0009-2363
PUBLISHER: Pharmaceutical Society of Japan
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A series of compds. structurally related to 2-phenyl-4'-(2,3,4,5-tetrahydro-1H-1,5-benzodiazepine-1-carbonyl)benzanilide was synthesized and demonstrated to have arginine vasopressin (AVP) antagonist activity for both V1A and V2 receptors. The introduction of a hydrophilic substituent group into the 5-position of the benzodiazepine ring resulted in an increase in oral availability. Esp., the (3-pyridyl)methyl, the 2-(4-methyl-1,4-diazepan-1-yl)-2-oxoethyl, and the 2-(4-methylpiperazin-1-yl)ethyl derivs. exhibited high antagonist activities and high oral availability. Details of the synthesis and pharmacol. properties of this series are presented.

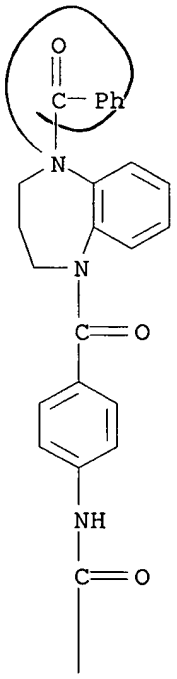
IT **217496-01-0P 217496-02-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of [[(benzodiazepinyl)carbonyl)]phenyl]biphenylcarboxamide derivs. as nonpeptide arginine vasopressin antagonists for both V1A and V2 receptors)

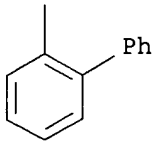
RN 217496-01-0 CAPLUS
CN [1,1'-Biphenyl]-2-carboxamide, N-[4-[(5-acetyl-2,3,4,5-tetrahydro-1H-1,5-benzodiazepin-1-yl)carbonyl]phenyl]- (9CI) (CA INDEX NAME)



RN 217496-02-1 CAPLUS
CN [1,1'-Biphenyl]-2-carboxamide, N-[4-[(5-benzoyl-2,3,4,5-tetrahydro-1H-1,5-benzodiazepin-1-yl)carbonyl]phenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



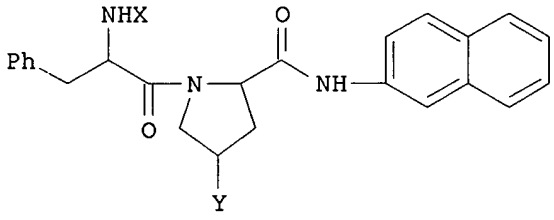


REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 20 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1998:268469 CAPLUS
DOCUMENT NUMBER: 129:16384
TITLE: Preparation of novel pyrrolidine derivatives as remedies for infectious diseases
INVENTOR(S): Ohta, Toshiharu; Nakayama, Kiyoshi; Ohtsuka, Masami; Inagaki, Hiroaki; Nishi, Toshiyuki; Ishida, Yohhei
PATENT ASSIGNEE(S): Daiichi Pharmaceutical Co., Ltd., Japan; Ohta, Toshiharu; Nakayama, Kiyoshi; Ohtsuka, Masami; Inagaki, Hiroaki
SOURCE: PCT Int. Appl., 164 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9817625	A1	19980430	WO 1997-JP3812	19971022
W: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GE, HU, ID, IL, IS, JP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9747221	A1	19980515	AU 1997-47221	19971022

PRIORITY APPLN. INFO.: JP 1996-279172 19961022
JP 1996-287203 19961030
WO 1997-JP3812 19971022
OTHER SOURCE(S): MARPAT 129:16384
GI



II

AB Novel compds. (I; R1-R3 = substituents in the cyclic structure, such as a pyrrolidine or a benzene ring; A = hydrocarbon or heterocyclo ring) are prepd. I act on pathogenic microorganisms which have acquired tolerance to the existing antimicrobials and elevate the sensitivity to the antimicrobials, thus making them nontolerant. When used together with the antimicrobials, I can efficaciously establish the prevention and treatment of microbial infectious diseases. Thus, compd. (II; X = tert-BuCO, Y = N3) (prepn. given) was hydrogenated over Pd/C to give 95% the title compd. II.2HCl (X = H, Y = NH2), which was tested and showed inhibitory activity against PAM1001.

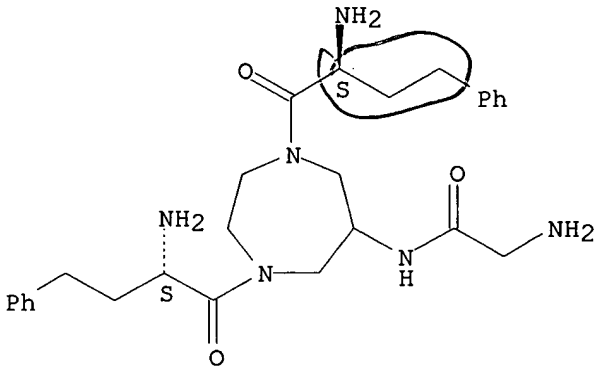
IT **207304-43-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of novel pyrrolidine derivs. as remedies for infectious diseases)

RN 207304-43-6 CAPLUS

CN Acetamide, 2-amino-N-[1,4-bis[(2S)-2-amino-1-oxo-4-phenylbutyl]hexahydro-1H-1,4-diazepin-6-yl]-, trihydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



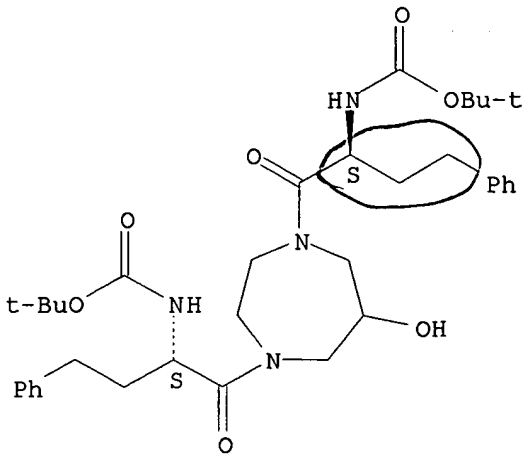
●3 HCl

IT **207305-43-9P 207305-44-0P 207305-45-1P**
207305-46-2P 207305-47-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of novel pyrrolidine derivs. as remedies for infectious diseases)

RN 207305-43-9 CAPLUS

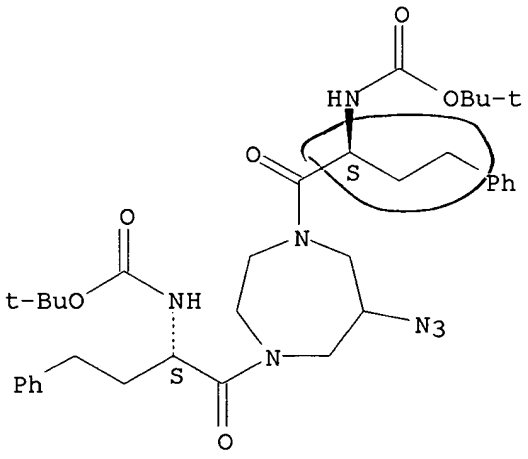
CN Carbamic acid, [(tetrahydro-6-hydroxy-1H-1,4-diazepine-1,4(5H)-diyl)bis[(1S)-2-oxo-1-(2-phenylethyl)-2,1-ethanediyl]]bis-, bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



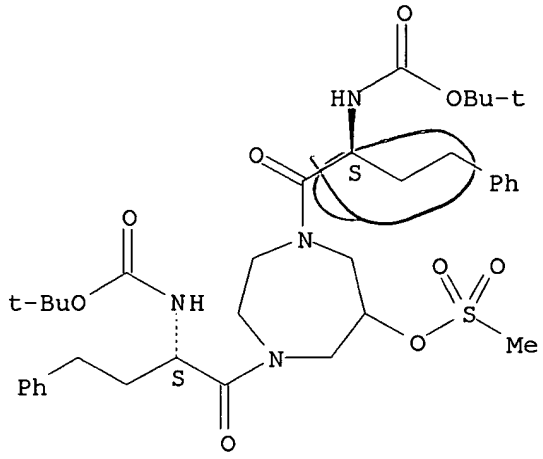
RN 207305-44-0 CAPLUS
CN Carbamic acid, [(6-azidotetrahydro-1H-1,4-diazepine-1,4(5H)-diyl)bis[(1S)-2-oxo-1-(2-phenylethyl)-2,1-ethanediyl]]bis-, bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



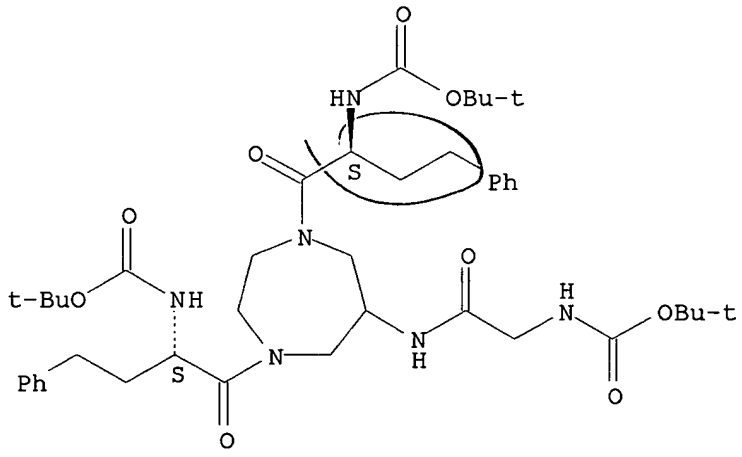
RN 207305-45-1 CAPLUS
CN Carbamic acid, [[tetrahydro-6-[(methylsulfonyl)oxy]-1H-1,4-diazepine-1,4(5H)-diyl]bis[(1S)-2-oxo-1-(2-phenylethyl)-2,1-ethanediyl]]bis-, bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



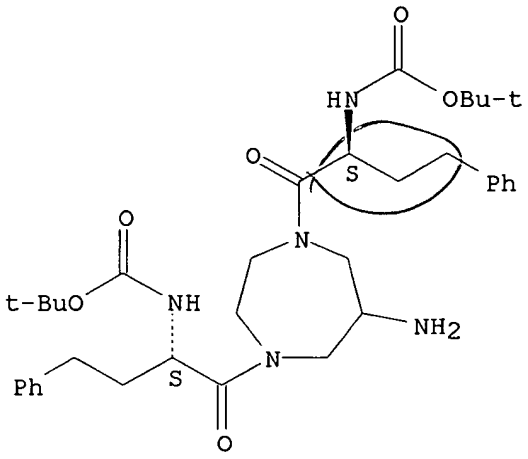
RN 207305-46-2 CAPLUS
CN Carbamic acid, [[6-[[[[(1,1-dimethylethoxy)carbonyl]amino]acetyl]amino]tetrahydro-1H-1,4-diazepine-1,4(5H)-diyl]bis[(1S)-2-oxo-1-(2-phenylethyl)-2,1-ethanediyl]]bis-, bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



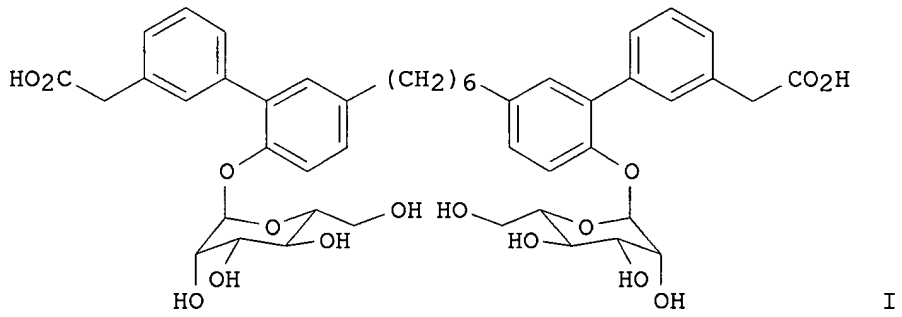
RN 207305-47-3 CAPLUS
CN Carbamic acid, [(6-aminotetrahydro-1H-1,4-diazepine-1,4(5H)-diyl)bis[(1S)-2-oxo-1-(2-phenylethyl)-2,1-ethanediyl]]bis-, bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 21 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1998:169713 CAPLUS
DOCUMENT NUMBER: 128:225679
TITLE: Novel Synthetic Inhibitors of Selectin-Mediated Cell Adhesion: Synthesis of 1,6-Bis[3-(3-carboxymethylphenyl)-4-(2-.alpha.-D-mannopyranosyloxy)phenyl]hexane (TBC1269)
AUTHOR(S): Kogan, Timothy P.; Dupre, Brian; Bui, Huong; McAbee, Kathy L.; Kassir, Jamal M.; Scott, Ian L.; Hu, Xin; Vanderslice, Peter; Beck, Pamela J.; Dixon, Richard A. F.
CORPORATE SOURCE: Departments of Chemistry Biophysics and Immunology, Texas Biotechnology Corporation, Houston, TX, 77030, USA
SOURCE: Journal of Medicinal Chemistry (1998), 41(7), 1099-1111
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

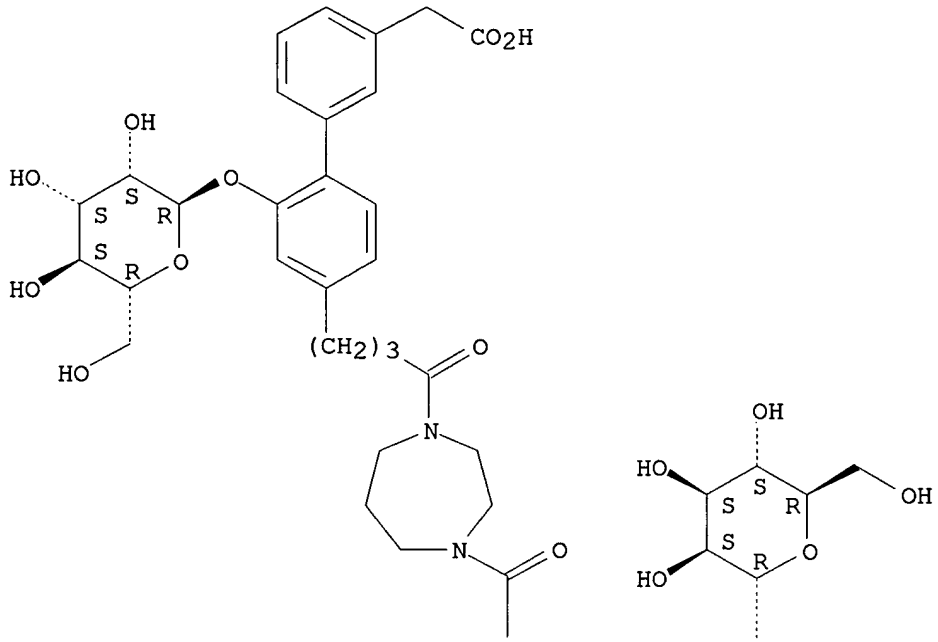
AB Reports of a high-affinity ligand for E-selectin, sialyl di-Lewisx motivated the authors to incorporate modifications to previously reported biphenyl-based inhibitors that would provide addnl. interactions with the protein. These compds. were assayed for the ability to inhibit the binding of sialyl Lewisx (sLex) bearing HL-60 cells to E-, P-, and L-selectin fusion proteins. The authors report that dimeric or trimeric compds. contg. multiple components of simple nonoligosaccharide selectin antagonists inhibit sLex-dependent binding with significantly enhanced potency over the monomeric compd. The enhanced potency is consistent with addnl. binding interactions within a single selectin lectin domain; however, multivalent interaction with multiple lectin domains as a possible alternative cannot be ruled out. Compd. I (TBC 1269) showed optimal in vitro activity from this class of antagonists and is currently under development for use in the treatment of asthma.

IT **204572-29-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of mannose-linked biphenylylacetic acid derivs. as novel inhibitors of selectin-mediated cell adhesion)
RN 204572-29-2 CAPLUS

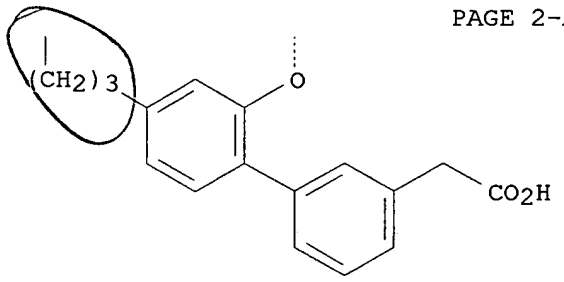
CN [1,1'-Biphenyl]-3-acetic acid, 4',4'''-[(tetrahydro-1H-1,4-diazepine-1,4(5H)-diyl)bis(4-oxo-4,1-butanediyl)]bis[2'-(.alpha.-D-mannopyranosyloxy)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A



applicants

L5 ANSWER 22 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1998:147312 CAPLUS
DOCUMENT NUMBER: 128:192678
TITLE: Preparation of diamide compounds as IgE production inhibitors
INVENTOR(S): Ishiwata, Hiroyuki; Kabeya, Mototsugu; Shigyo, Hiromichi; Shiratsuchi, Masami; Hattori, Yukio; Nakao, Hiroshi; Nagoya, Takao; Sato, Seiichi; Oda, Soichi; et al.
PATENT ASSIGNEE(S): Kowa Co., Ltd., Japan; Ishiwata, Hiroyuki; Kabeya, Mototsugu; Shigyo, Hiromichi; Shiratsuchi, Masami; Hattori, Yukio; Nakao, Hiroshi; Nagoya, Takao; Sato, Seiichi
SOURCE: PCT Int. Appl., 93 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9807702	A1	19980226	WO 1997-JP2882	19970820
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9738668	A1	19980306	AU 1997-38668	19970820
EP 926138	A1	19990630	EP 1997-935832	19970820
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
US 6340682	B1	20020122	US 1999-147711	19990223
US 2002042414	A1	20020411	US 2001-978102	20011017

PRIORITY APPLN. INFO.: JP 1996-222770 A 19960823
WO 1997-JP2882 W 19970820
US 1999-147711 A3 19990223
OTHER SOURCE(S): MARPAT 128:192678

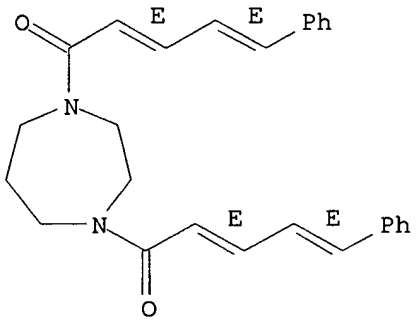
AB Diamide derivs. ABCOWCOBA [A represents optionally substituted Ph, etc.; B represents CH:CH, C.tplbond.C, phenylene, etc.; and W represents 1,4,8-triazabicyclo[4,4,0]decane, etc.] are prepd. The title compds. are useful as antiallergic agents, etc. Thus, 1,4-bis[5-phenylpenta-(2E,4E)-dienoyl]hexahydro-1,4-diazepine at 10-5 M gave 100% inhibition of IgE prodn. in B cells.

IT **203721-07-7P 203721-08-8P 203721-09-9P**
203721-11-3P 203721-12-4P 203721-13-5P
203721-14-6P 203721-15-7P 203721-16-8P
203721-17-9P 203721-18-0P 203721-19-1P
203721-20-4P 203721-21-5P 203721-22-6P
203721-23-7P 203721-24-8P 203721-25-9P
203721-26-0P 203721-27-1P 203721-28-2P
203721-29-3P 203721-30-6P 203721-31-7P
203721-32-8P 203721-54-4P 203721-55-5P
203721-56-6P 203721-57-7P 203721-71-5P
203721-72-6P 203721-73-7P 203721-74-8P

203721-75-9P 203721-76-0P 203721-77-1P
203721-78-2P 203721-81-7P 203721-82-8P
203721-83-9P 203721-84-0P 203721-86-2P
203721-89-5P 203721-92-0P 203721-93-1P
203721-94-2P 203721-95-3P 203721-96-4P
203721-97-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of diamide compds. as IgE prodn. inhibitors)

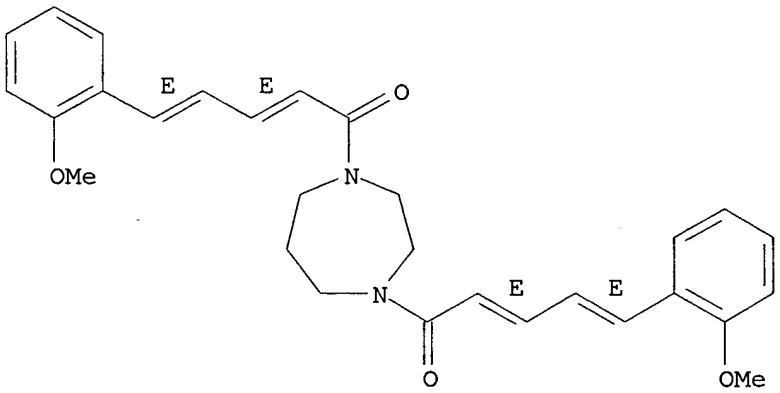
RN 203721-07-7 CAPLUS
CN 1H-1,4-Diazepine, hexahydro-1,4-bis(1-oxo-5-phenyl-2,4-pentadienyl)-, (all-E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



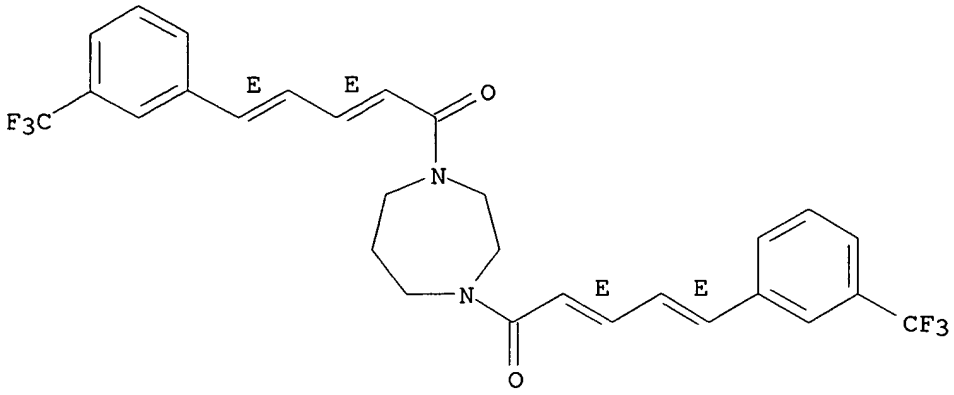
RN 203721-08-8 CAPLUS
CN 1H-1,4-Diazepine, hexahydro-1,4-bis[5-(2-methoxyphenyl)-1-oxo-2,4-pentadienyl]-, (all-E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



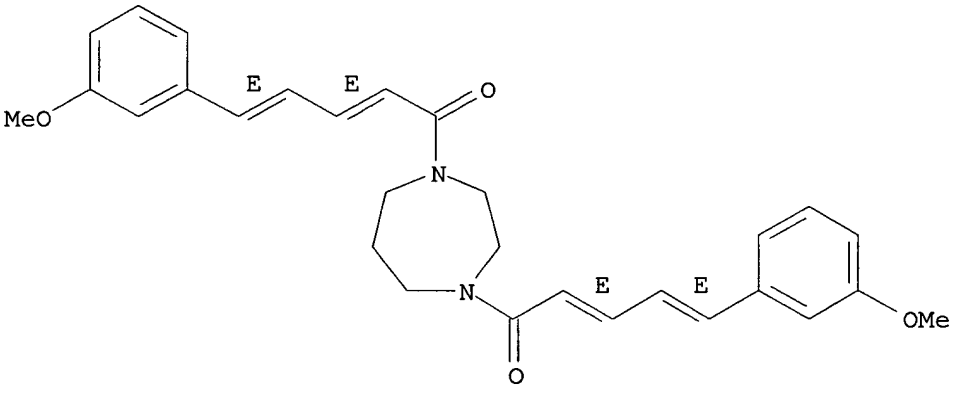
RN 203721-09-9 CAPLUS
CN 1H-1,4-Diazepine, hexahydro-1,4-bis[1-oxo-5-[3-(trifluoromethyl)phenyl]-2,4-pentadienyl]-, (all-E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



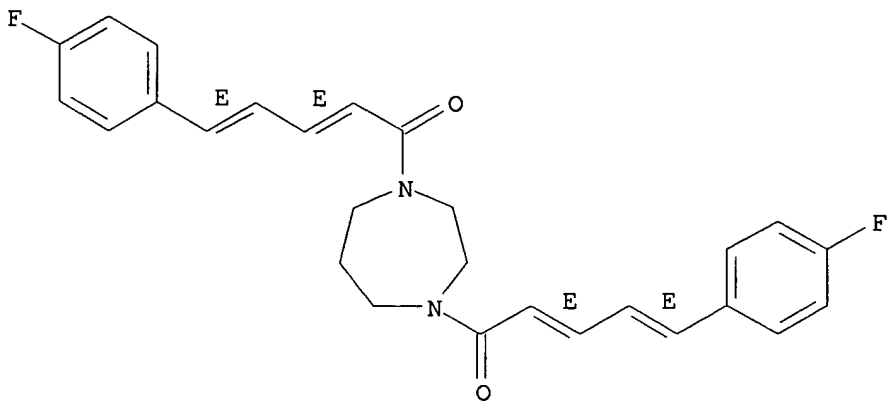
RN 203721-11-3 CAPLUS
CN 1H-1,4-Diazepine, hexahydro-1,4-bis[5-(3-methoxyphenyl)-1-oxo-2,4-pentadienyl]-, (all-E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



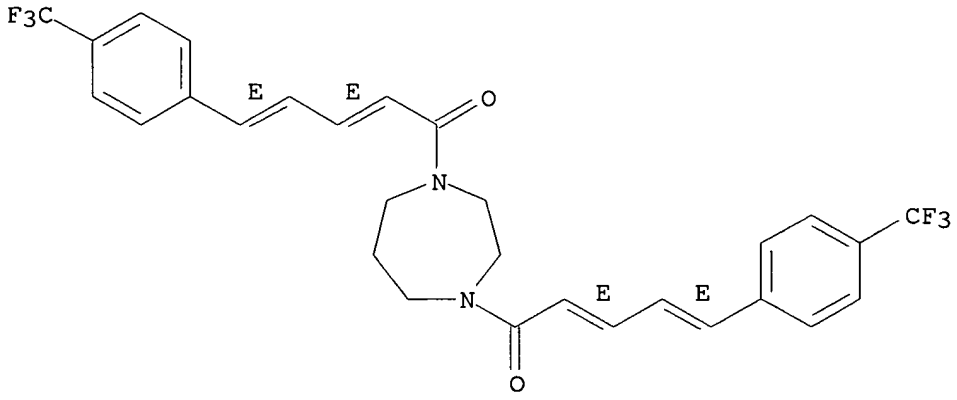
RN 203721-12-4 CAPLUS
CN 1H-1,4-Diazepine, 1,4-bis[5-(4-fluorophenyl)-1-oxo-2,4-pentadienyl]hexahydro-, (all-E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



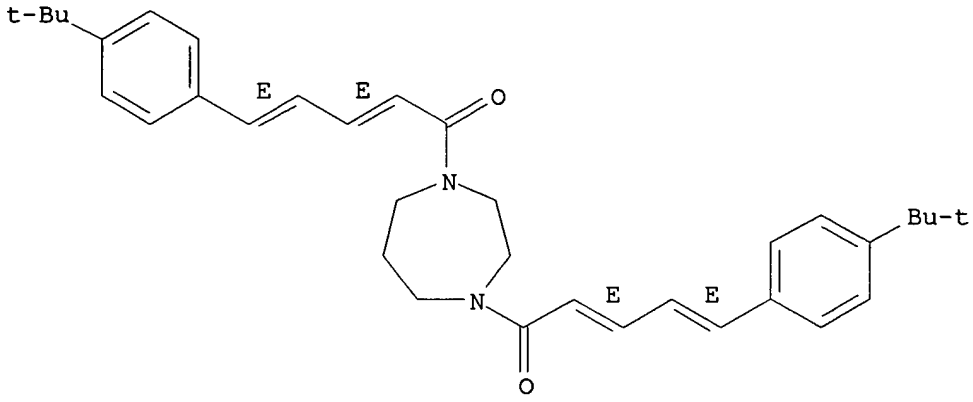
RN 203721-13-5 CAPLUS
CN 1H-1,4-Diazepine, hexahydro-1,4-bis[1-oxo-5-[4-(trifluoromethyl)phenyl]-2,4-pentadienyl]-, (all-E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



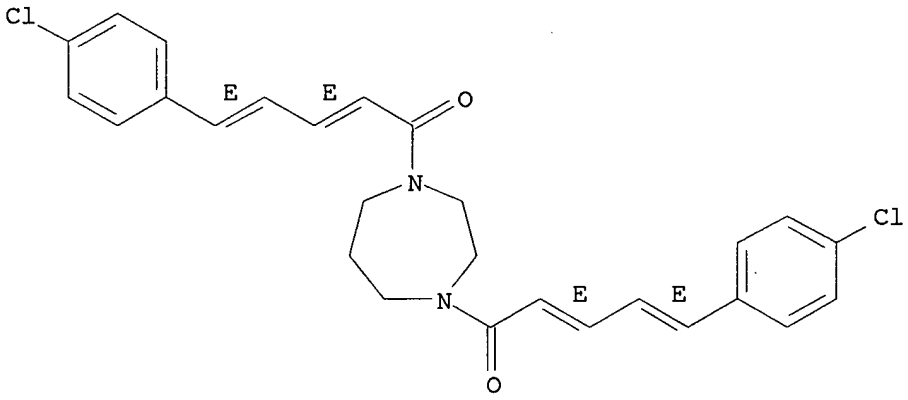
RN 203721-14-6 CAPLUS
CN 1H-1,4-Diazepine, 1,4-bis[5-[4-(1,1-dimethylethyl)phenyl]-1-oxo-2,4-pentadienyl]hexahydro-, (all-E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 203721-15-7 CAPLUS
CN 1H-1,4-Diazepine, 1,4-bis[5-(4-chlorophenyl)-1-oxo-2,4-pentadienyl]hexahydro-, (all-E)- (9CI) (CA INDEX NAME)

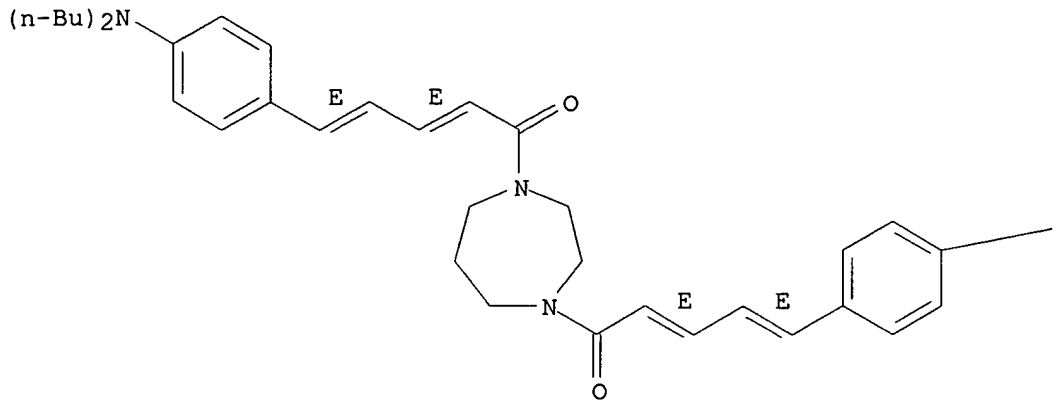
Double bond geometry as shown.



RN 203721-16-8 CAPLUS
CN 1H-1,4-Diazepine, 1,4-bis[5-[4-(dibutylamino)phenyl]-1-oxo-2,4-pentadienyl]hexahydro-, dihydrochloride, (all-E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



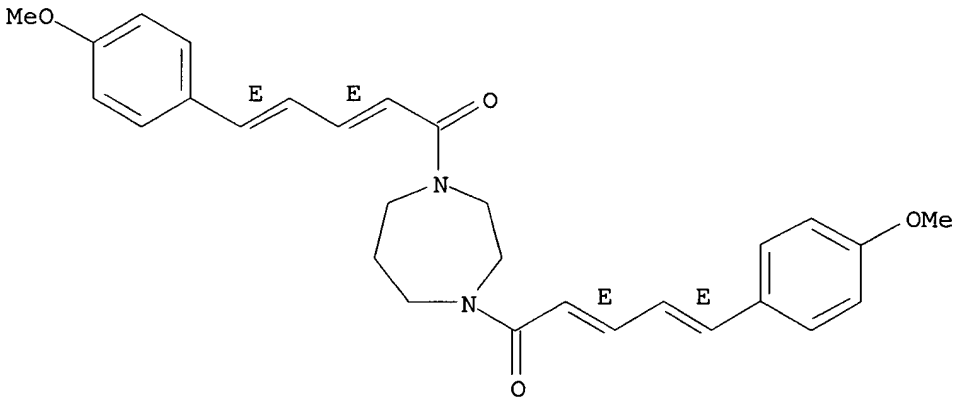
●2 HCl

PAGE 1-B

—N(Bu-n)2

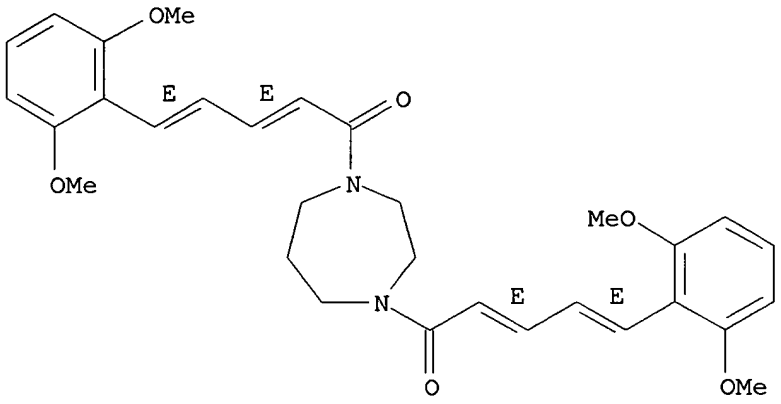
RN 203721-17-9 CAPLUS
CN 1H-1,4-Diazepine, hexahydro-1,4-bis[5-(4-methoxyphenyl)-1-oxo-2,4-pentadienyl]-, (all-E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



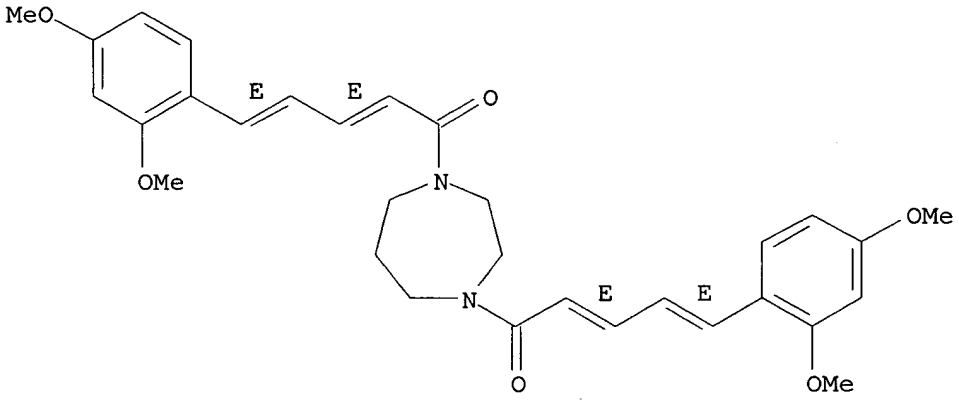
RN 203721-18-0 CAPLUS
CN 1H-1,4-Diazepine, 1,4-bis[5-(2,6-dimethoxyphenyl)-1-oxo-2,4-pentadienyl]hexahydro-, (all-E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



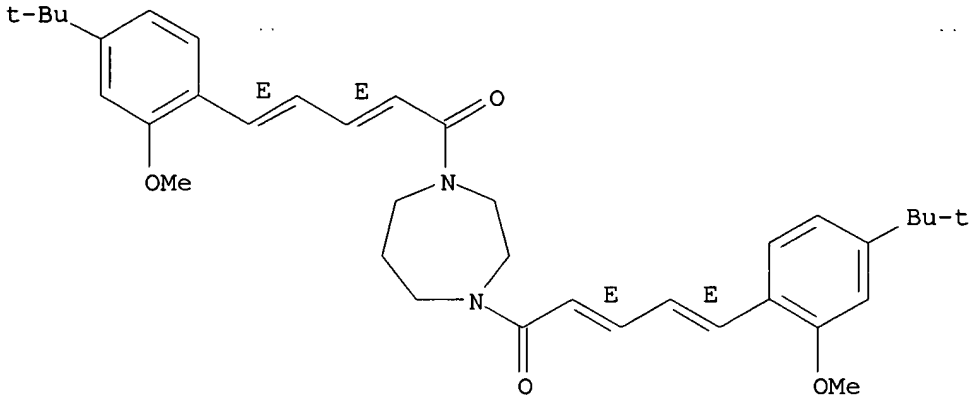
RN 203721-19-1 CAPLUS
CN 1H-1,4-Diazepine, 1,4-bis[5-(2,4-dimethoxyphenyl)-1-oxo-2,4-pentadienyl]hexahydro-, (all-E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



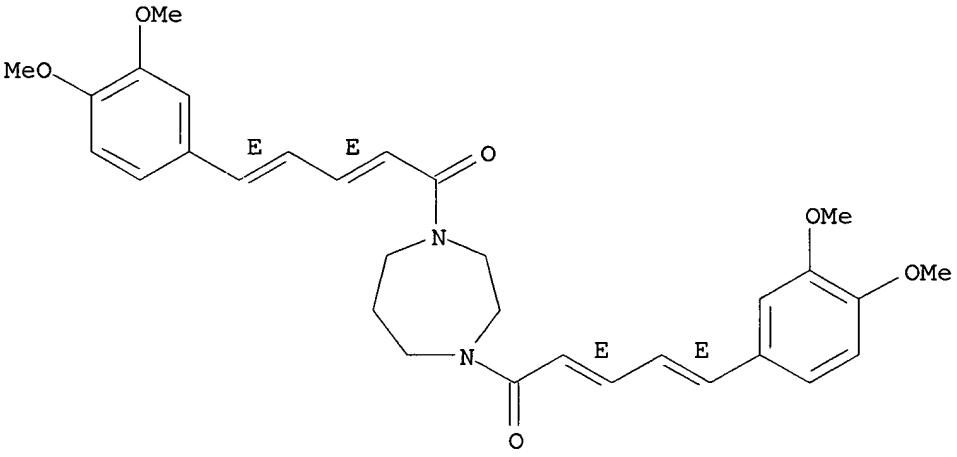
RN 203721-20-4 CAPLUS
CN 1H-1,4-Diazepine, 1,4-bis[5-[4-(1,1-dimethylethyl)-2-methoxyphenyl]-1-oxo-2,4-pentadienyl]hexahydro-, (all-E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



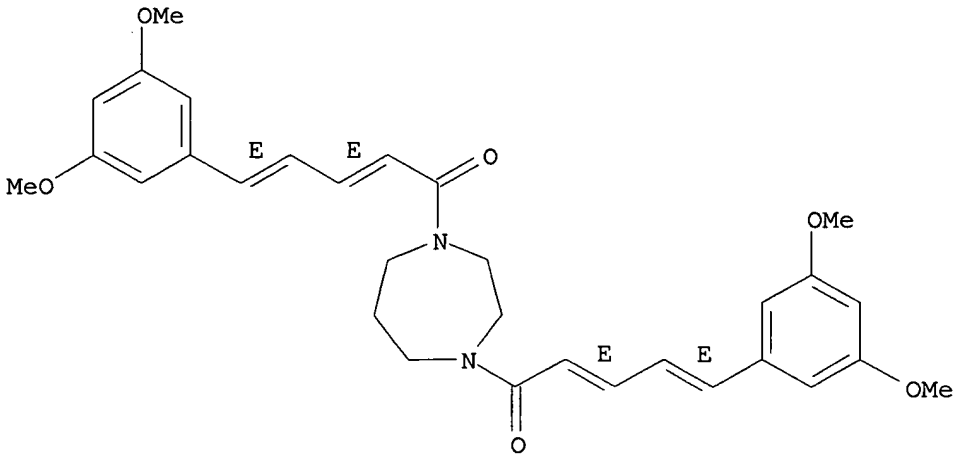
RN 203721-21-5 CAPLUS
CN 1H-1,4-Diazepine, 1,4-bis[5-(3,4-dimethoxyphenyl)-1-oxo-2,4-pentadienyl]hexahydro-, (all-E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



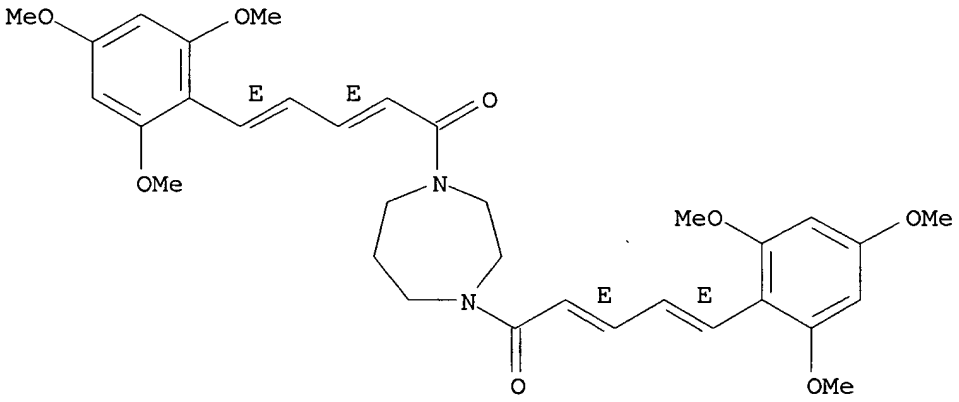
RN 203721-22-6 CAPLUS
CN 1H-1,4-Diazepine, 1,4-bis[5-(3,5-dimethoxyphenyl)-1-oxo-2,4-pentadienyl]hexahydro-, (all-E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



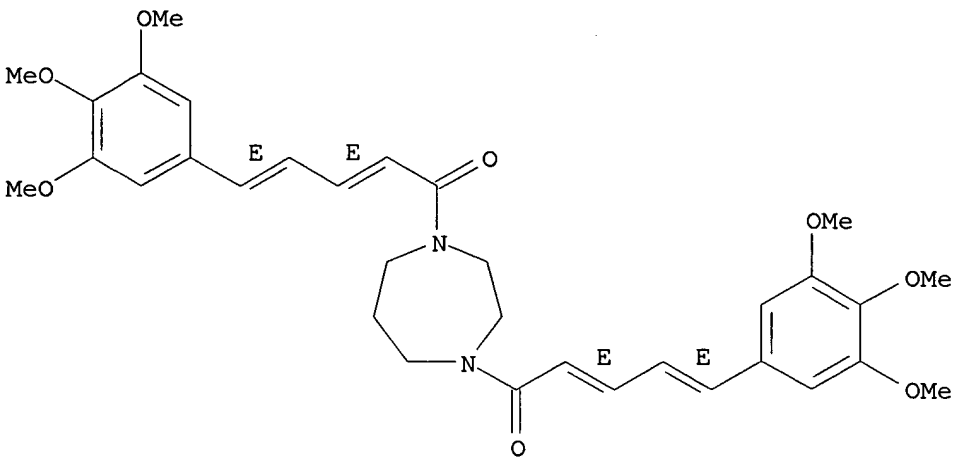
RN 203721-23-7 CAPLUS
CN 1H-1,4-Diazepine, hexahydro-1,4-bis[1-oxo-5-(2,4,6-trimethoxyphenyl)-2,4-pentadienyl]-, (all-E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



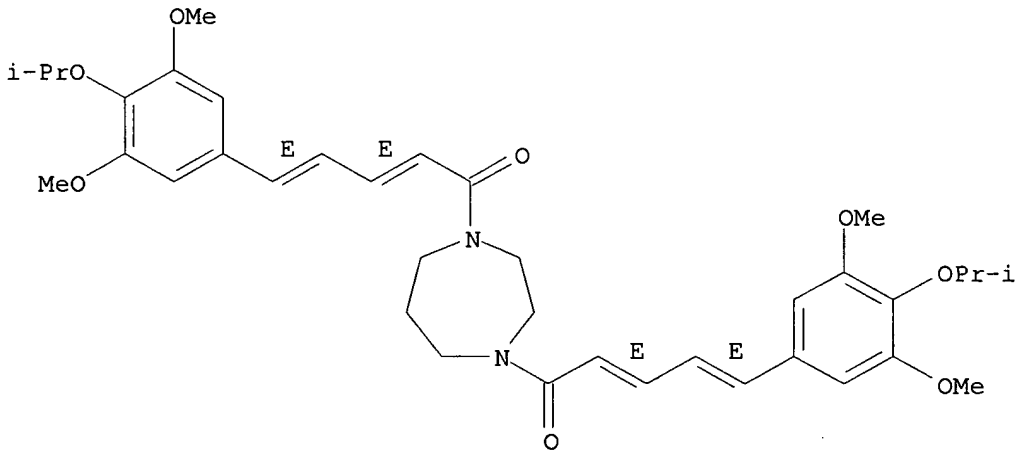
RN 203721-24-8 CAPLUS
CN 1H-1,4-Diazepine, hexahydro-1,4-bis[1-oxo-5-(3,4,5-trimethoxyphenyl)-2,4-pentadienyl]-, (all-E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



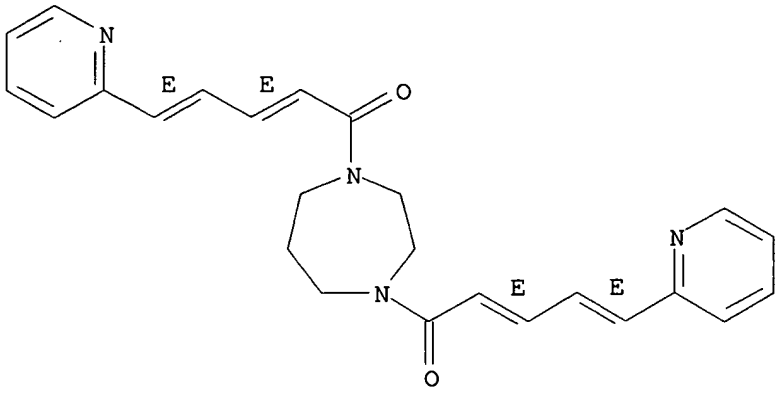
RN 203721-25-9 CAPLUS
CN 1H-1,4-Diazepine, 1,4-bis[5-[3,5-dimethoxy-4-(1-methylethoxy)phenyl]-1-oxo-2,4-pentadienyl]hexahydro-, (all-E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



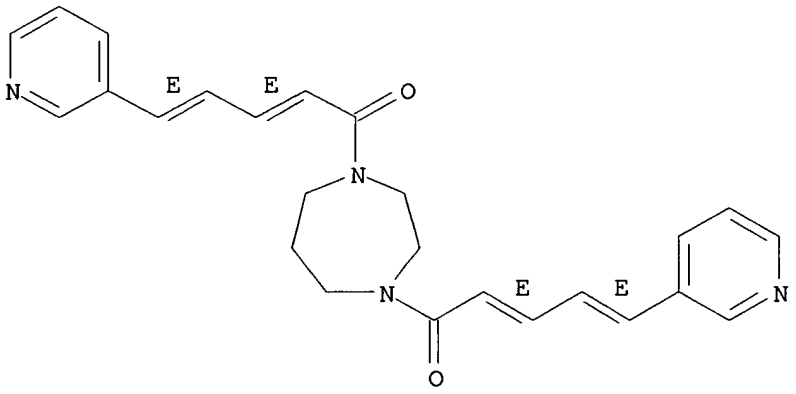
RN 203721-26-0 CAPLUS
CN 1H-1,4-Diazepine, hexahydro-1,4-bis[1-oxo-5-(2-pyridinyl)-2,4-pentadienyl]-, (all-E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



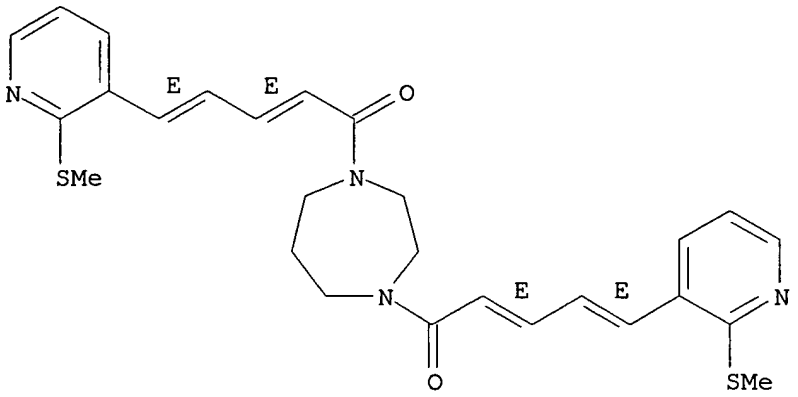
RN 203721-27-1 CAPLUS
CN 1H-1,4-Diazepine, hexahydro-1,4-bis[1-oxo-5-(3-pyridinyl)-2,4-pentadienyl]-, (all-E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



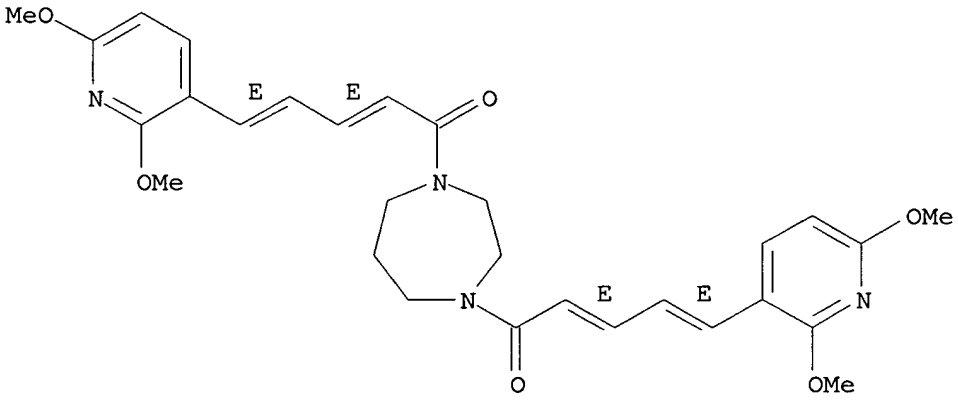
RN 203721-28-2 CAPLUS
CN 1H-1,4-Diazepine, hexahydro-1,4-bis[5-[2-(methylthio)-3-pyridinyl]-1-oxo-2,4-pentadienyl]-, (all-E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



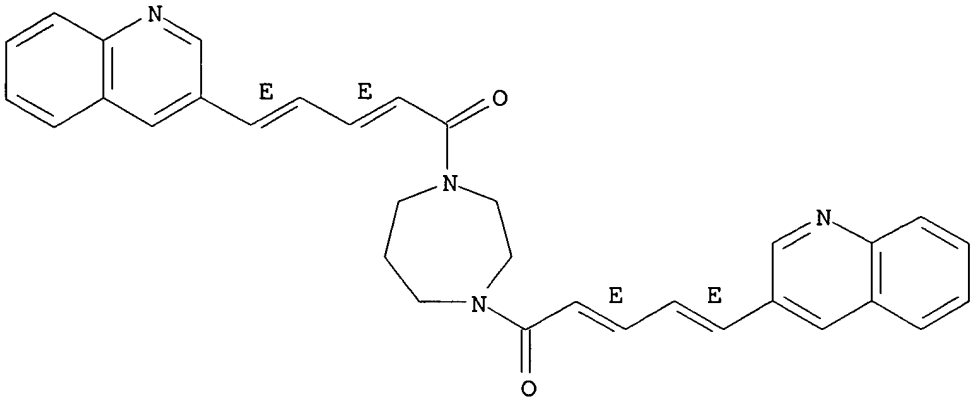
RN 203721-29-3 CAPLUS
CN 1H-1,4-Diazepine, 1,4-bis[5-(2,6-dimethoxy-3-pyridinyl)-1-oxo-2,4-pentadienyl]hexahydro-, (all-E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



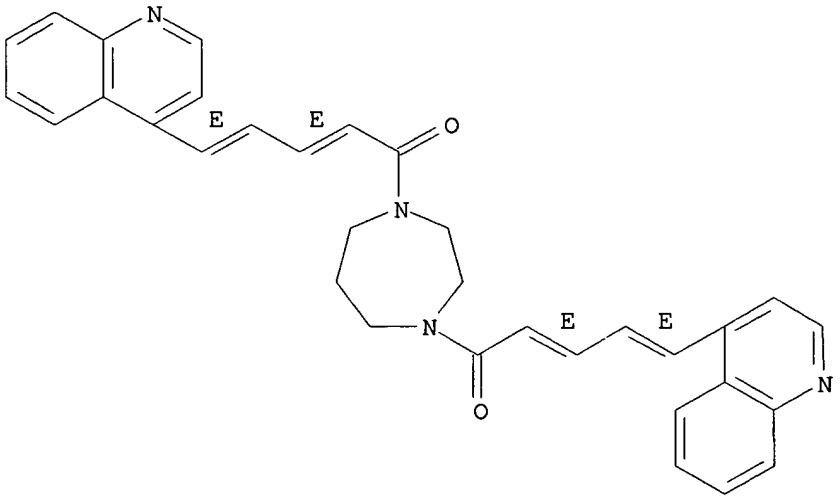
RN 203721-30-6 CAPLUS
CN 1H-1,4-Diazepine, hexahydro-1,4-bis[1-oxo-5-(3-quinolinyl)-2,4-pentadienyl]-, (all-E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



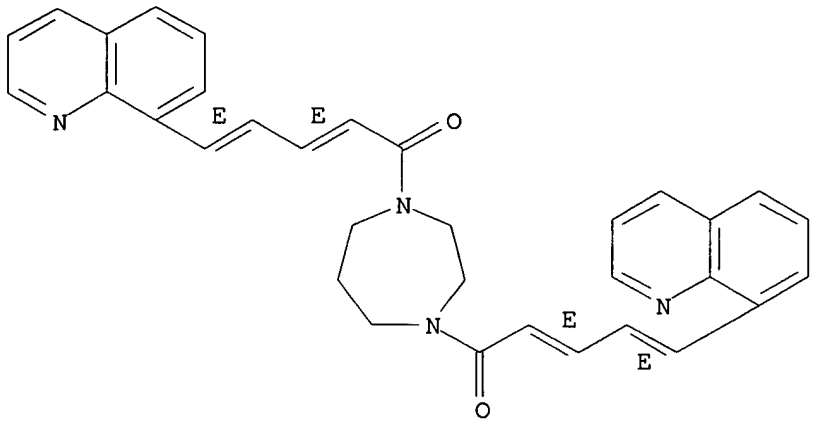
RN 203721-31-7 CAPLUS
CN 1H-1,4-Diazepine, hexahydro-1,4-bis[1-oxo-5-(4-quinolinyl)-2,4-pentadienyl]-, (all-E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



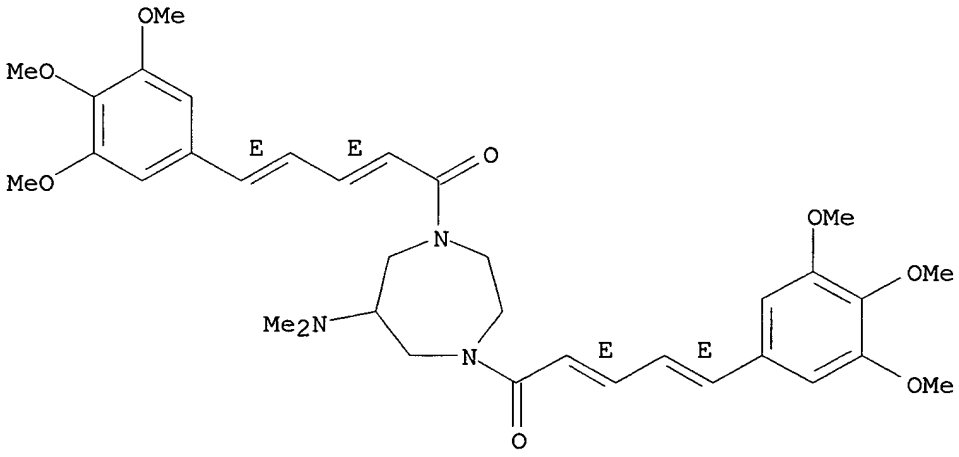
RN 203721-32-8 CAPLUS
CN 1H-1,4-Diazepine, hexahydro-1,4-bis[1-oxo-5-(8-quinolinyl)-2,4-pentadienyl]-, (all-E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



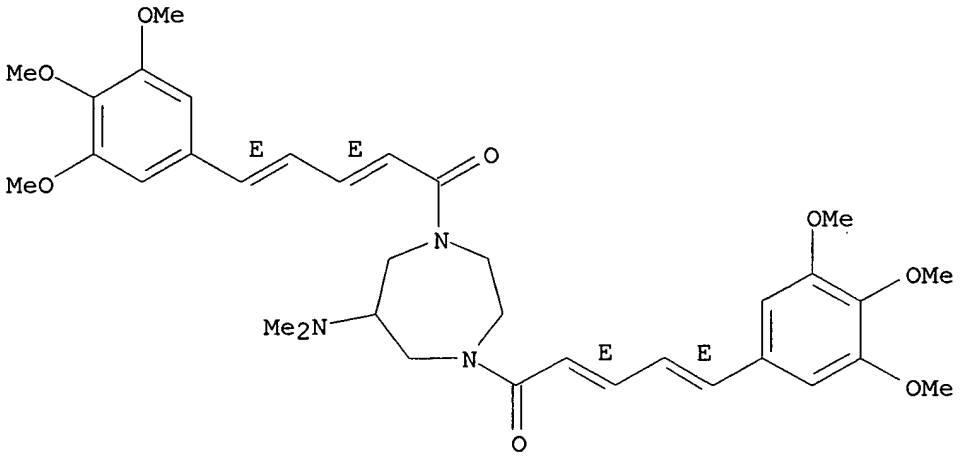
RN 203721-54-4 CAPLUS
CN 1H-1,4-Diazepin-6-amine, hexahydro-N,N-dimethyl-1,4-bis[1-oxo-5-(3,4,5-trimethoxyphenyl)-2,4-pentadienyl]-, (all-E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 203721-55-5 CAPLUS
CN 1H-1,4-Diazepin-6-amine, hexahydro-N,N-dimethyl-1,4-bis[1-oxo-5-(3,4,5-trimethoxyphenyl)-2,4-pentadienyl]-, monohydrochloride, (all-E)- (9CI) (CA INDEX NAME)

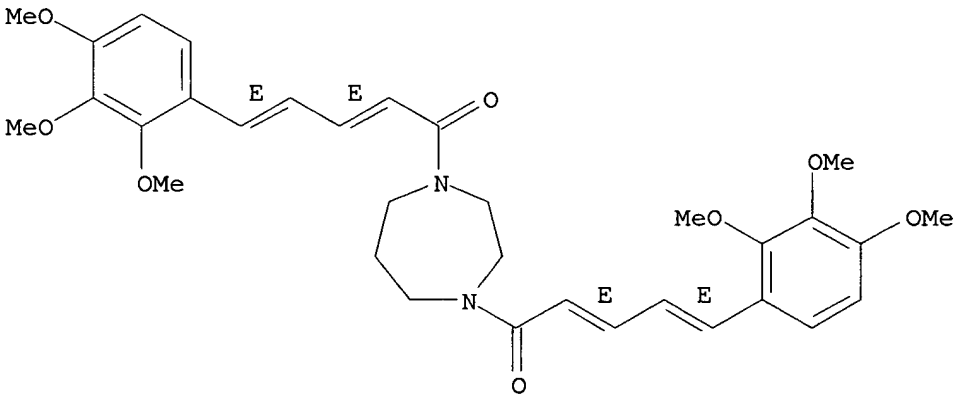
Double bond geometry as shown.



● HCl

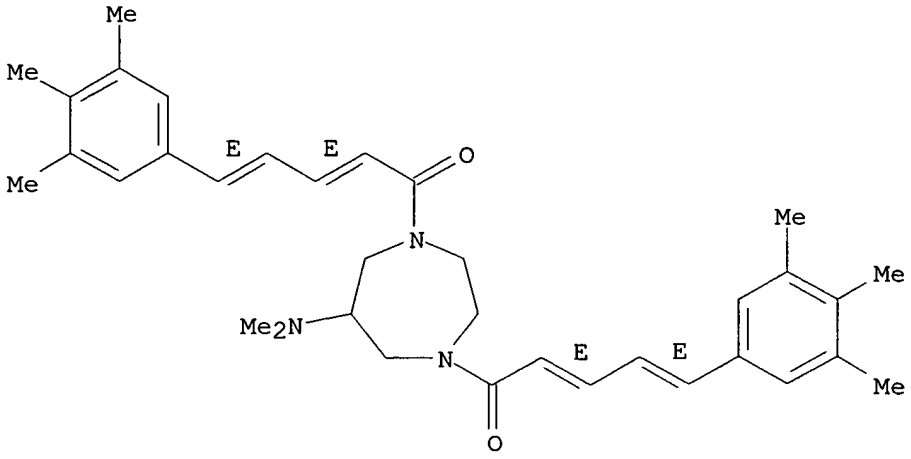
RN 203721-56-6 CAPLUS
CN 1H-1,4-Diazepine, hexahydro-1,4-bis[1-oxo-5-(2,3,4-trimethoxyphenyl)-2,4-pentadienyl]-, (all-E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



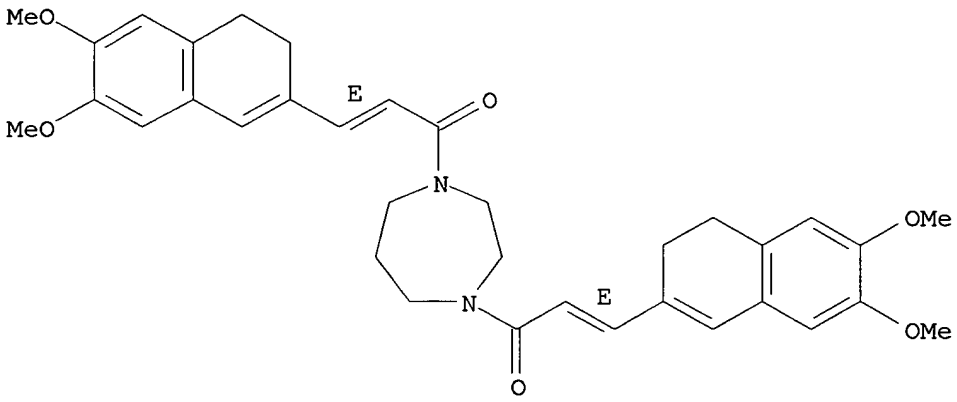
RN 203721-57-7 CAPLUS
CN 1H-1,4-Diazepin-6-amine, hexahydro-N,N-dimethyl-1,4-bis[1-oxo-5-(3,4,5-trimethylphenyl)-2,4-pentadienyl]-, (all-E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



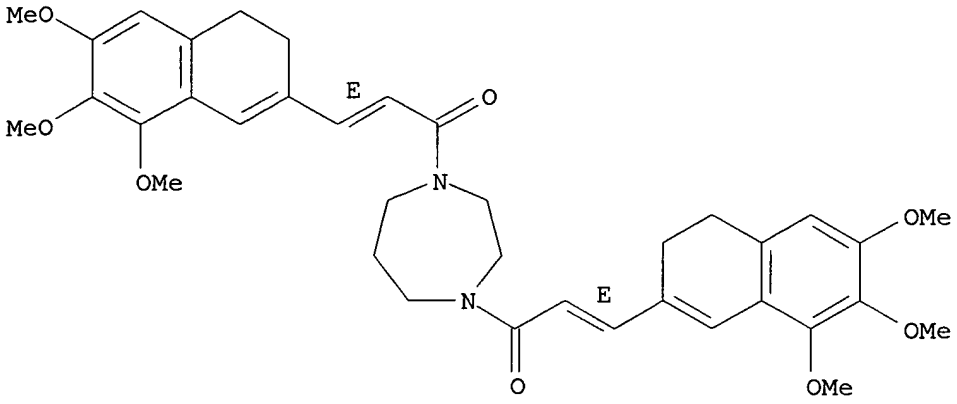
RN 203721-71-5 CAPLUS
CN 1H-1,4-Diazepine, 1,4-bis[3-(3,4-dihydro-6,7-dimethoxy-2-naphthalenyl)-1-oxo-2-propenyl]hexahydro-, (E,E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



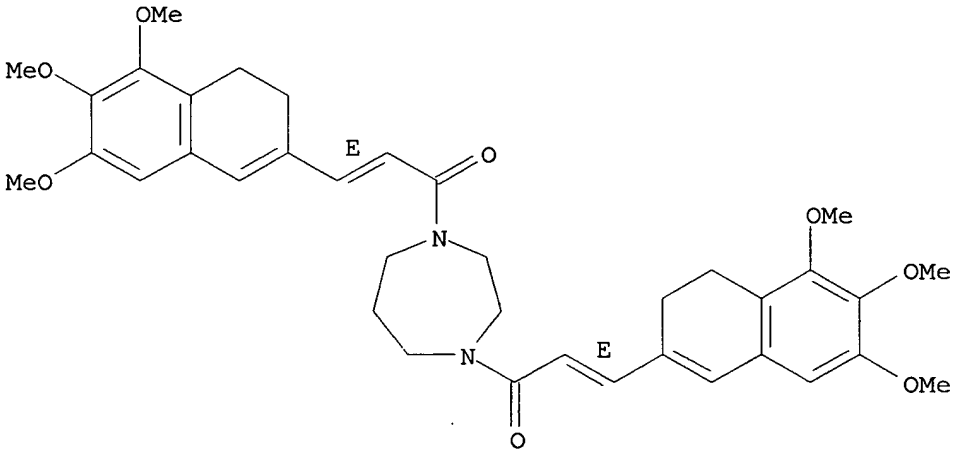
RN 203721-72-6 CAPLUS
CN 1H-1,4-Diazepine, 1,4-bis[3-(3,4-dihydro-6,7,8-trimethoxy-2-naphthalenyl)-1-oxo-2-propenyl]hexahydro-, (E,E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



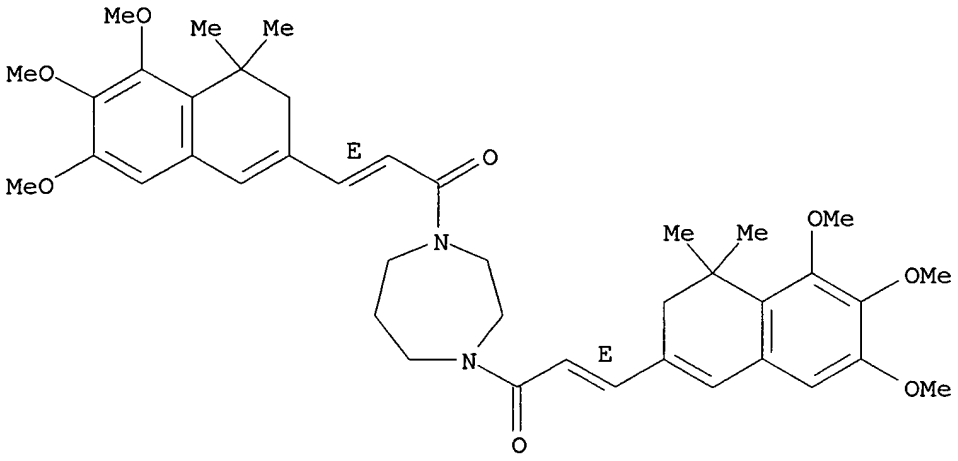
RN 203721-73-7 CAPLUS
CN 1H-1,4-Diazepine, 1,4-bis[3-(3,4-dihydro-5,6,7-trimethoxy-2-naphthalenyl)-1-oxo-2-propenyl]hexahydro-, (E,E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



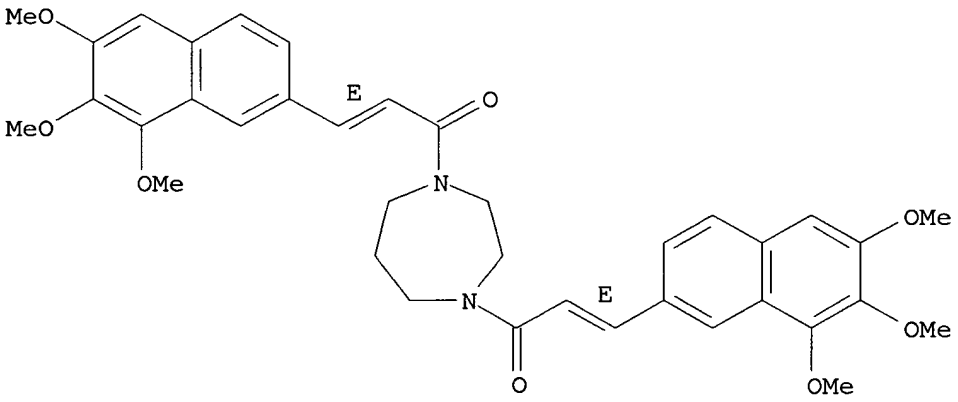
RN 203721-74-8 CAPLUS
CN 1H-1,4-Diazepine, 1,4-bis[3-(3,4-dihydro-5,6,7-trimethoxy-4,4-dimethyl-2-naphthalenyl)-1-oxo-2-propenyl]hexahydro-, (E,E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



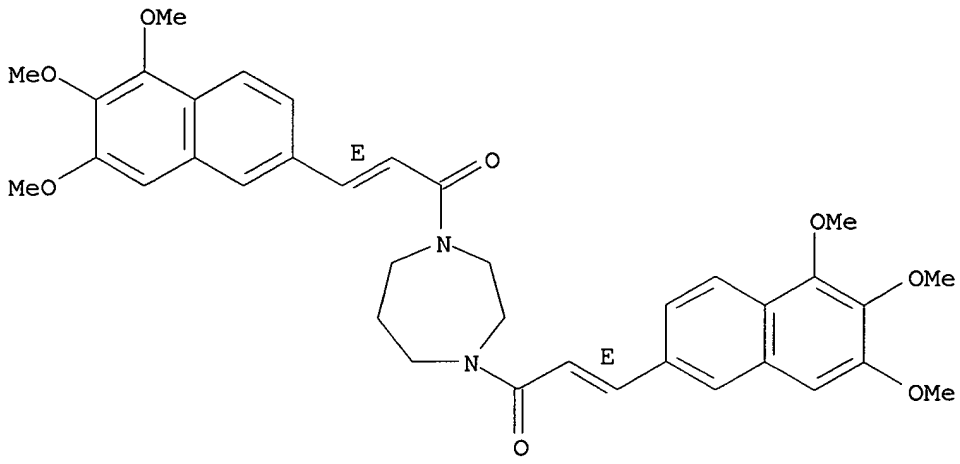
RN 203721-75-9 CAPLUS
CN 1H-1,4-Diazepine, hexahydro-1,4-bis[1-oxo-3-(6,7,8-trimethoxy-2-naphthalenyl)-2-propenyl]-, (E,E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



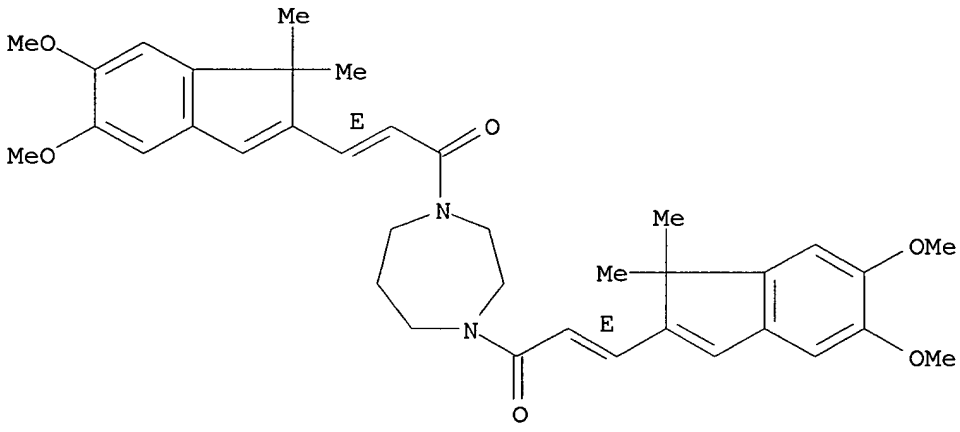
RN 203721-76-0 CAPLUS
CN 1H-1,4-Diazepine, hexahydro-1,4-bis[1-oxo-3-(5,6,7-trimethoxy-2-naphthalenyl)-2-propenyl]-, (E,E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



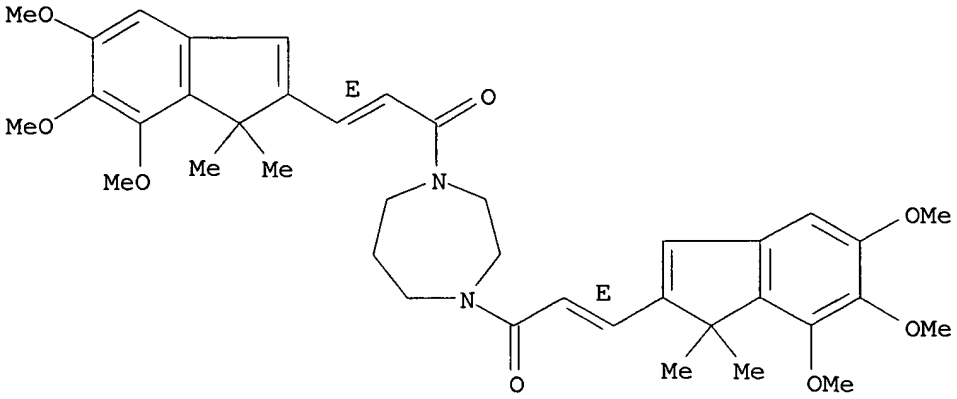
RN 203721-77-1 CAPLUS
CN 1H-1,4-Diazepine, 1,4-bis[3-(5,6-dimethoxy-1,1-dimethyl-1H-inden-2-yl)-1-oxo-2-propenyl]hexahydro-, (E,E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

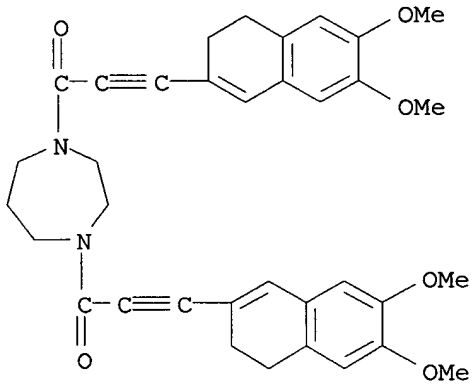


RN 203721-78-2 CAPLUS
CN 1H-1,4-Diazepine, hexahydro-1,4-bis[1-oxo-3-(5,6,7-trimethoxy-1,1-dimethyl-1H-inden-2-yl)-2-propenyl]-, (E,E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

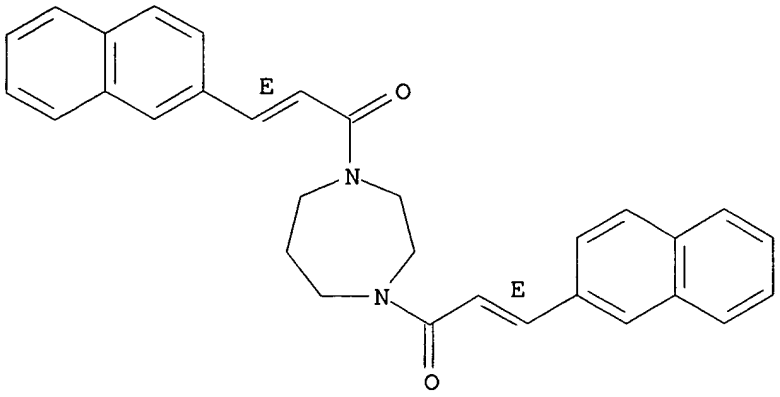


RN 203721-81-7 CAPLUS
CN 1H-1,4-Diazepine, 1,4-bis[3-(3,4-dihydro-6,7-dimethoxy-2-naphthalenyl)-1-oxo-2-propynyl]hexahydro- (9CI) (CA INDEX NAME)



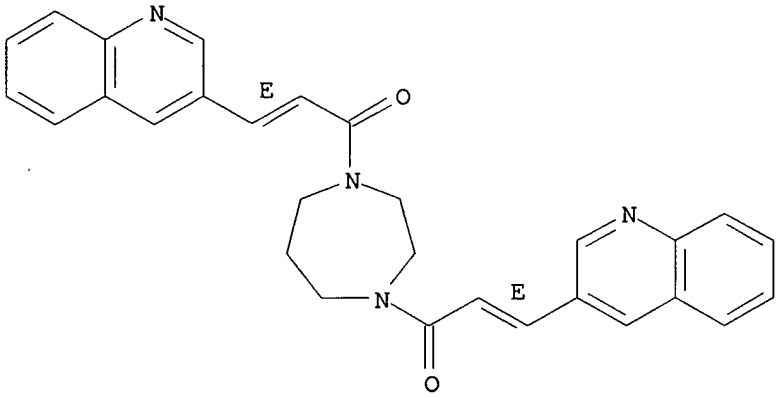
RN 203721-82-8 CAPLUS
CN 1H-1,4-Diazepine, hexahydro-1,4-bis[3-(2-naphthalenyl)-1-oxo-2-propenyl]-, (E,E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

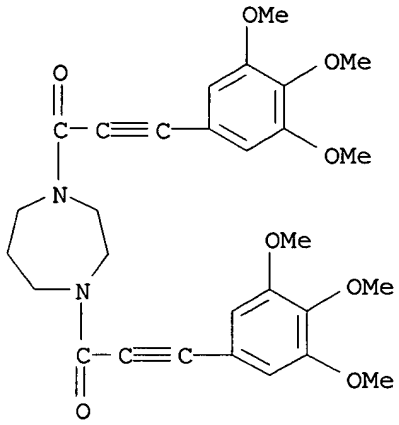


RN 203721-83-9 CAPLUS
CN 1H-1,4-Diazepine, hexahydro-1,4-bis[1-oxo-3-(3-quinolinyl)-2-propenyl]-, (E,E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

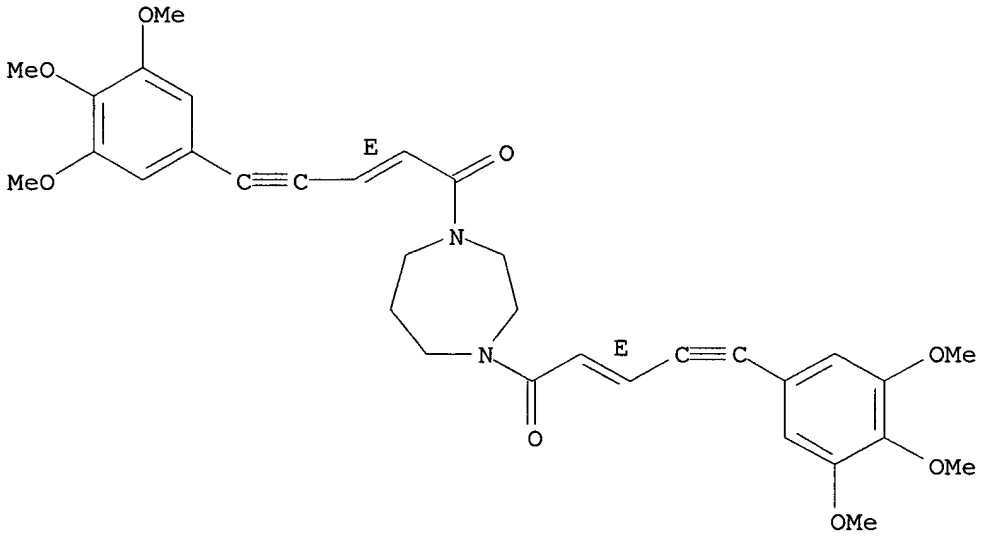


RN 203721-84-0 CAPLUS
CN 1H-1,4-Diazepine, hexahydro-1,4-bis[1-oxo-3-(3,4,5-trimethoxyphenyl)-2-propynyl]- (9CI) (CA INDEX NAME)



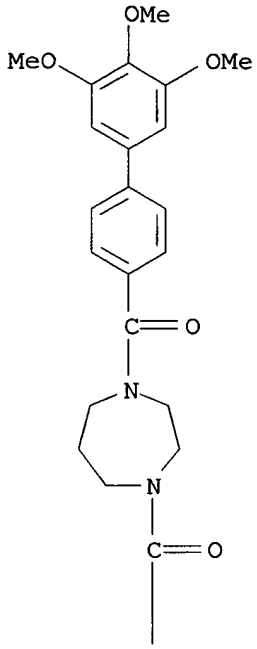
RN 203721-86-2 CAPLUS
CN 1H-1,4-Diazepine, hexahydro-1,4-bis[1-oxo-5-(3,4,5-trimethoxyphenyl)-2-penten-4-ynyl]-, (E,E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

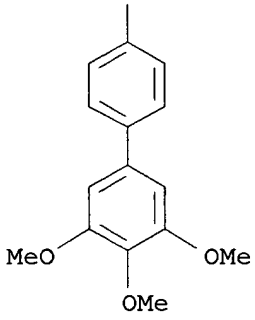


RN 203721-89-5 CAPLUS
CN 1H-1,4-Diazepine, hexahydro-1,4-bis[(3',4',5'-trimethoxy[1,1'-biphenyl]-4-yl)carbonyl]- (9CI) (CA INDEX NAME)

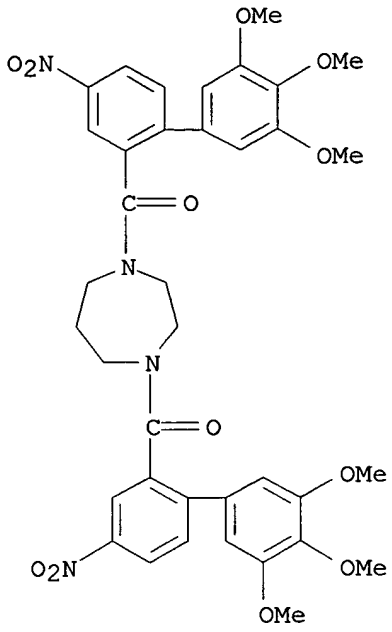
PAGE 1-A



PAGE 2-A

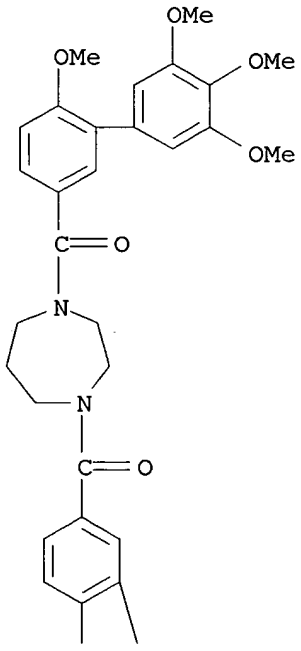


RN 203721-92-0 CAPLUS
CN 1H-1,4-Diazepine, hexahydro-1,4-bis[(3',4',5'-trimethoxy-4-nitro[1,1'-biphenyl]-2-yl)carbonyl]- (9CI) (CA INDEX NAME)

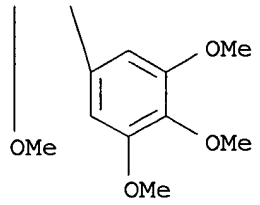


RN 203721-93-1 CAPLUS
CN 1H-1,4-Diazepine, hexahydro-1,4-bis[(3',4',5',6-tetramethoxy[1,1'-biphenyl]-3-yl)carbonyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

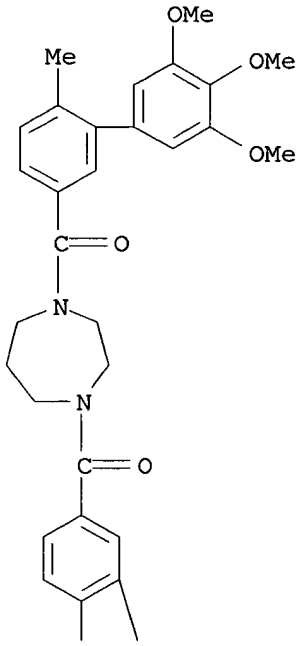


PAGE 2-A



RN 203721-94-2 CAPLUS
CN 1H-1,4-Diazepine, hexahydro-1,4-bis[(3',4',5'-trimethoxy-6-methyl[1,1'-biphenyl]-3-yl)carbonyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



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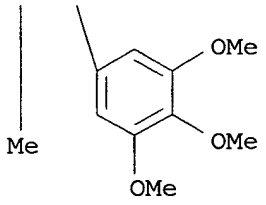
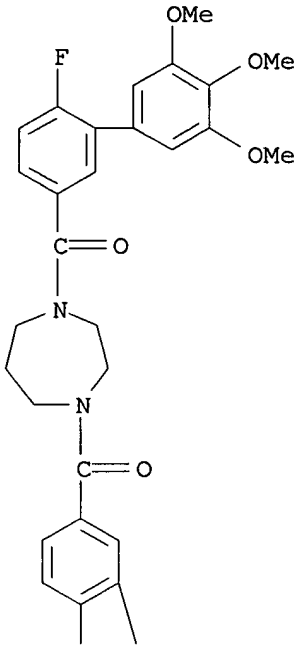
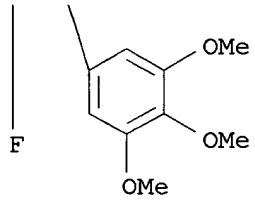


RN 203721-95-3 CAPLUS
CN 1H-1,4-Diazepine, 1,4-bis[(6-fluoro-3',4',5'-trimethoxy[1,1'-biphenyl]-3-yl)carbonyl]hexahydro- (9CI) (CA INDEX NAME)

PAGE 1-A

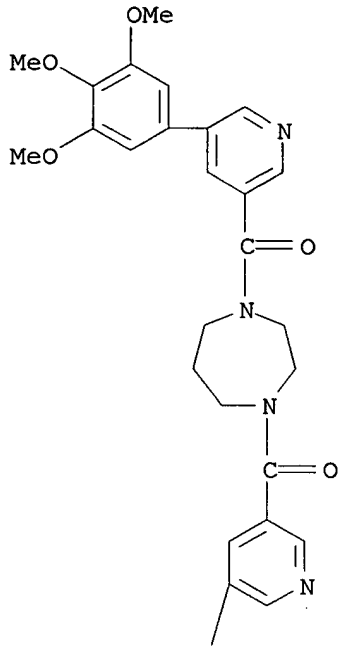


PAGE 2-A

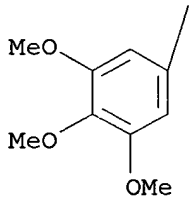


RN 203721-96-4 CAPLUS
CN 1H-1,4-Diazepine, hexahydro-1,4-bis[[5-(3,4,5-trimethoxyphenyl)-3-pyridinyl]carbonyl]- (9CI) (CA INDEX NAME)

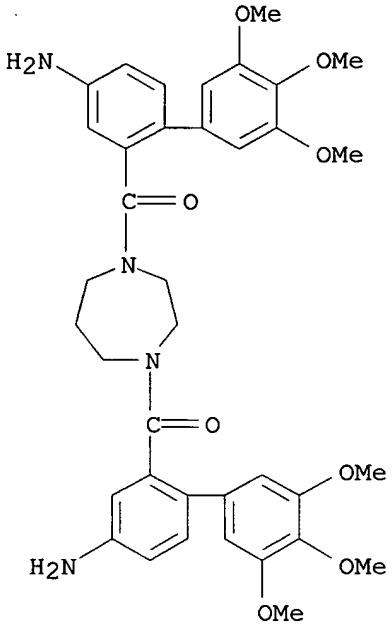
PAGE 1-A



PAGE 2-A



RN 203721-97-5 CAPLUS
CN 1H-1,4-Diazepine, 1,4-bis[(4-amino-3',4',5'-trimethoxy[1,1'-biphenyl]-2-yl)carbonyl]hexahydro- (9CI) (CA INDEX NAME)



IT **203721-98-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of diamide compds. as IgE prodn. inhibitors)
RN 203721-98-6 CAPLUS
CN 1H-1,4-Diazepine, 1,4-bis[5-[4-(dibutylamino)phenyl]-1-oxo-2,4-pentadienyl]hexahydro-, (all-E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

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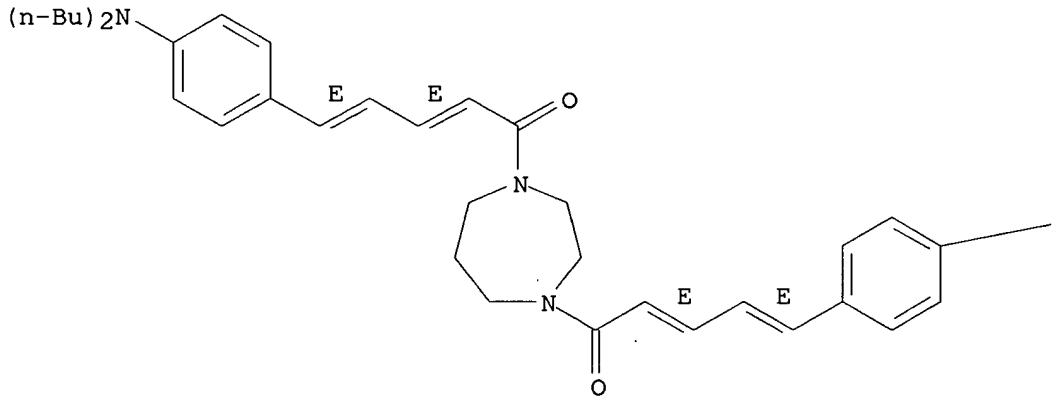


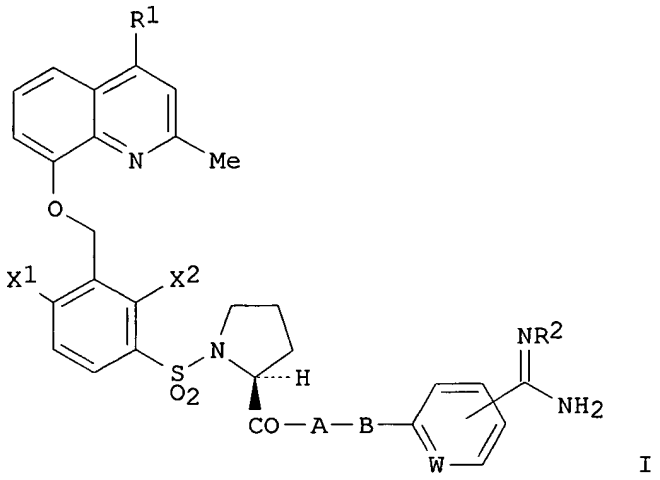
—N(Bu-n)2

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 23 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1998:87728 CAPLUS
DOCUMENT NUMBER: 128:154381
TITLE: Preparation of N-benzenesulfonyl-L-proline derivatives as bradykinin B2 agonists
INVENTOR(S): Dodey, Pierre; Bondoux, Michel; Houziaux, Patrick; Barth, Martine; Ou, Khan
PATENT ASSIGNEE(S): Fournier Industrie et Sante, Fr.; Dodey, Pierre; Bondoux, Michel; Houziaux, Patrick; Barth, Martine; Ou, Khan
SOURCE: PCT Int. Appl., 72 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9803503	A1	19980129	WO 1997-FR1377	19970723
W: AU, BG, BR, CA, CN, CZ, EE, HU, IL, JP, KR, MX, NO, NZ, PL, RO, RU, SG, SK, TR, UA, US, VN				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
FR 2751650	A1	19980130	FR 1996-9327	19960724
FR 2751650	B1	19981009		
CA 2261743	AA	19980129	CA 1997-2261743	19970723
AU 9738536	A1	19980210	AU 1997-38536	19970723
EP 925295	A1	19990630	EP 1997-935612	19970723
EP 925295	B1	20011004		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, RO				
JP 2000514818	T2	20001107	JP 1998-506663	19970723
AT 206419	E	20011015	AT 1997-935612	19970723
ES 2167768	T3	20020516	ES 1997-935612	19970723
US 6071917	A	20000606	US 1999-230334	19990125

PRIORITY APPLN. INFO.: FR 1996-9327 A 19960724
WO 1997-FR1377 W 19970723
OTHER SOURCE(S): MARPAT 128:154381
GI



I

AB N-benzenesulfonyl-L-proline derivs. I [X1, X2 = halo, alkoxy; R1 = H, trifluoroalkyl, alkyl; R2 = H, OH; A = NR3(CH2)n (R3 = H, Me and n = 0-3), 1,4-piperazinediyl, hexahydro-1,4-diazepine-1,4-diyl; NH(CH2)nCH(CH2CH2)2N [n = 0-3, CH(CH2CH2)2N = 1,4-piperazinediyl]; B = bond, CO, COCH2, COCH2O, COCH:CH, SO2; W = CH, N] or their salts were prepd. as bradykinin B2 agonists. Thus, I.2HCl (X1 = X2 = Cl, R1 = Me, R2 = H, A = NHCH2, B = bond, W = CH; the amidino group is in the 3-position) was prepd. from N-[[3-[(2,4-dimethylquinolin-8-yl)oxymethyl]-2,4-dichlorophenyl]sulfonyl]-L-proline by sequential reaction with H2S, MeI, NH4OAc, and HCl. The product inhibited binding of [3H] bradykinin to the B2 receptor in guinea pigs (100% activity).

IT **202602-71-9P 202720-72-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of benzenesulfonylproline derivs. as bradykinin B2 agonists)

RN 202602-71-9 CAPLUS

CN 1H-1,4-Diazepine, 1-[4-(aminoiminomethyl)benzoyl]-4-[[(2S)-1-[[2,4-dichloro-3-[[(2,4-dimethyl-8-quinolinyl)oxy]methyl]phenyl]sulfonyl]-2-pyrrolidinyl]carbonyl]hexahydro- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

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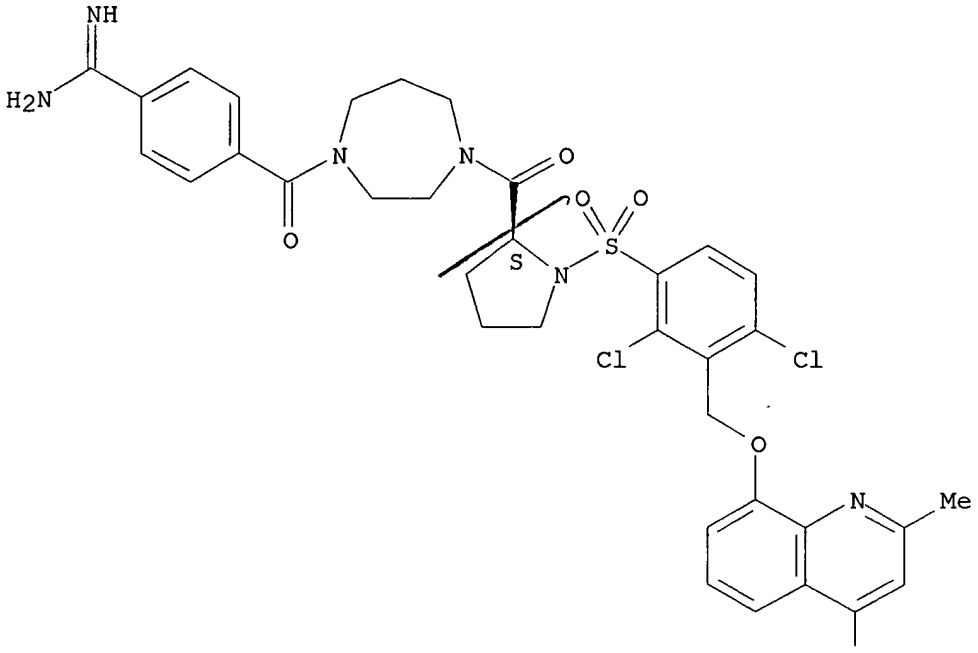

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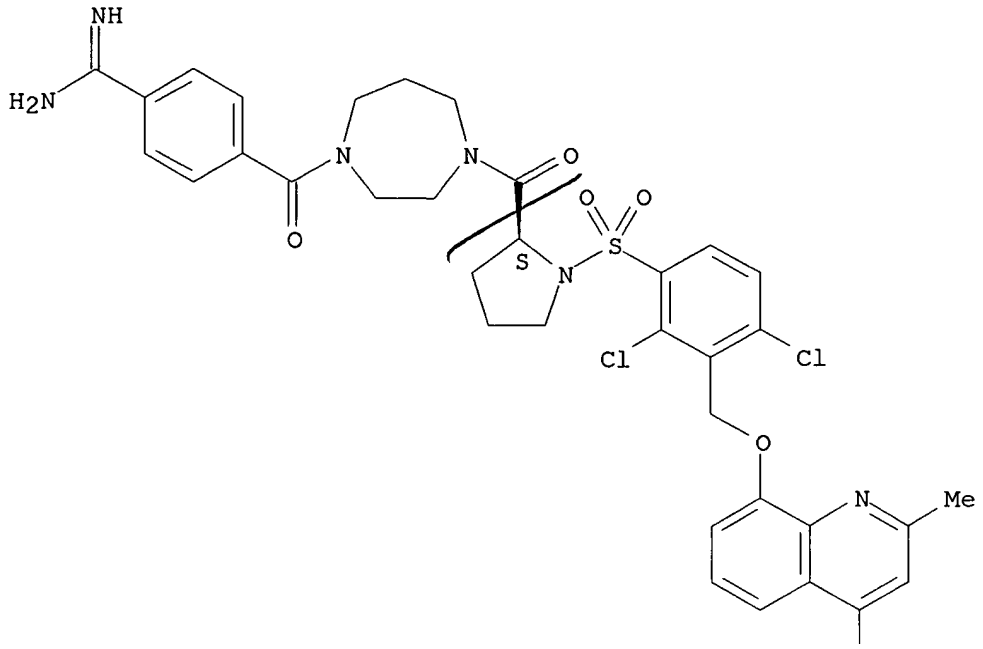
RN 202720-72-7 CAPLUS
CN 1H-1,4-Diazepine, 1-[4-(aminoiminomethyl)benzoyl]-4-[[1-[[2,4-dichloro-3-[[(2,4-dimethyl-8-quinolinyl)oxy]methyl]phenyl]sulfonyl]-2-pyrrolidinyl]carbonyl]hexahydro-, dihydrochloride, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

PAGE 1-A



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●2 HCl

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 24 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1997:579715 CAPLUS
DOCUMENT NUMBER: 127:278213
TITLE: Imidazole-containing benzodiazepines and analogs as inhibitors of farnesyl protein transferase
INVENTOR(S): Ding, Charles Z.; Hunt, John T.; Kim, Soong-hoon; Mitt, Toomis; Bhide, Rajeev; Leftheris, Katerina
PATENT ASSIGNEE(S): Bristol-Myers Squibb Co., USA
SOURCE: PCT Int. Appl., 425 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9730992	A1	19970828	WO 1997-US2920	19970224
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 6011029	A	20000104	US 1997-802329	19970220
AU 9721366	A1	19970910	AU 1997-21366	19970224
AU 718676	B2	20000420		
EP 892797	A1	19990127	EP 1997-906761	19970224
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
CN 1214685	A	19990421	CN 1997-192535	19970224
BR 9707614	A	19990727	BR 1997-7614	19970224
JP 2000502356	T2	20000229	JP 1997-530395	19970224
NZ 330287	A	20000327	NZ 1997-330287	19970224
ZA 9701621	A	19980825	ZA 1997-1621	19970225
LV 12150	B	19981220	LV 1998-129	19980604
NO 9803892	A	19980825	NO 1998-3892	19980825
LT 4552	B	19991025	LT 1998-120	19980825
US 6455523	B1	20020924	US 1999-374210	19990813
CN 1347881	A	20020508	CN 2001-141154	20010927

PRIORITY APPLN. INFO.:
US 1996-12265P P 19960226
US 1996-22805P P 19960725
US 1997-802329 A3 19970220
WO 1997-US2920 W 19970224

OTHER SOURCE(S): MARPAT 127:278213
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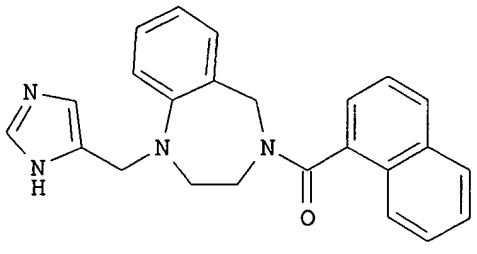


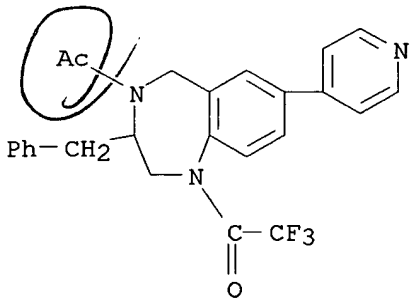
I

AB The invention relates to a series of imidazole-substituted benzodiazepines and analogs that inhibit farnesyl-protein transferase (FPT) and ras protein farnesylation, thereby being useful as anti-cancer agents. The compds. are also useful in the treatment of diseases, other than cancer, assocd. with signal transduction pathways operating through ras, and those assocd. with proteins other than ras that are also post-translationally modified by FPT. The compds. may also act as inhibitors of other prenyl transferases, and thus be effective in the treatment of diseases assocd. with other prenyl modifications of proteins. Over 430 synthetic examples are given. For instance, 2,3,4,5-tetrahydro-1H-1,4-benzodiazepine was N-acylated by 1-naphthoic acid Ph ester in the presence of DMAP, and the product was reductively alkylated by 4-formylimidazole in the presence of NaBH(OAc)3 to give title compd. I, isolated as the HCl salt. The example compds. inhibited FPT with IC50 values between 0.1 nM and 100 .mu.M.

IT **195985-42-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; prepn. of imidazole-contg. benzodiazepines and analogs as inhibitors of farnesyl protein transferase)

RN 195985-42-3 CAPLUS

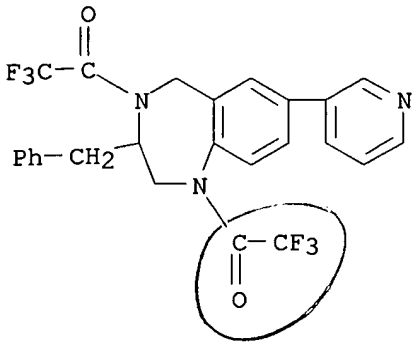
CN 1H-1,4-Benzodiazepine, 4-acetyl-2,3,4,5-tetrahydro-3-(phenylmethyl)-7-(4-pyridinyl)-1-(trifluoroacetyl)- (9CI) (CA INDEX NAME)



IT **195987-11-2**
RL: RCT (Reactant); RACT (Reactant or reagent)
(starting material; prepn. of imidazole-contg. benzodiazepines and analogs as inhibitors of farnesyl protein transferase)

RN 195987-11-2 CAPLUS

CN 1H-1,4-Benzodiazepine, 2,3,4,5-tetrahydro-3-(phenylmethyl)-7-(3-pyridinyl)-1,4-bis(trifluoroacetyl)- (9CI) (CA INDEX NAME)



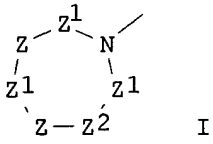
L5 ANSWER 25 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1997:527643 CAPLUS
DOCUMENT NUMBER: 127:190761
TITLE: Preparation of amide-linked bis(DOTA) compounds as contrast agent chelants
INVENTOR(S): Carvalho, Joan; Watson, Alan D.; Fellmann, Jere D.; Koo, Michael David
PATENT ASSIGNEE(S): Nycomed Salutar, USA
SOURCE: U.S., 19 pp., Cont.-in-part of U.S. Ser. No. 855,028, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5650133	A	19970722	US 1994-226760	19940412
US 5281704	A	19940125	US 1990-468107	19900119
JP 2000136174	A2	20000516	JP 1999-192219	19901020
US 5446145	A	19950829	US 1993-86996	19930707
CA 2172735	AA	19950413	CA 1994-2172735	19940929
CN 1136313	A	19961120	CN 1994-194300	19940929
CN 1045772	B	19991020		
HU 74592	A2	19970128	HU 1996-805	19940929
US 5972307	A	19991026	US 1997-898376	19970722

PRIORITY APPLN. INFO.:

US 1990-468107	A2	19900119
US 1992-855028	B2	19920612
US 1993-86996	A2	19930707
GB 1993-20277	A	19931001
GB 1989-23843	A	19891023
JP 1990-515144	A3	19901020
US 1992-885028	B2	19920612
US 1994-226760	A3	19940412

OTHER SOURCE(S): MARPAT 127:190761
GI



I

AB [R(CH2)q]2Z3 [R = polyaza macrocyclic group I; .gtoreq.2 of Z = NR2 and the others = NR2, O, S; R2 = R1 or CR12R3; R1 = H, (hydroxy)alkyl, alkoxyalkyl; R3 = CO2H, SO3H, PO3H, etc.; Z1 = (CR12)2-3; Z2 = (Z1Z)m; Z3 = bridging group; m = 0-2; q = 1 or 2] and Gd complexes thereof were prepd. Thus, (CH2NHMe)2 was bisalkylated by BrCH2COBr and the product bisamidated by RH [R = I, Z = NCH2CO2R4, Z1 = CH2CH2, Z2 = CH2CH2N(CH2CO2R4)](II; R4 = CMe3)(prepn. given) to give, after deprotection, (CH2NMeCH2COR)2 (R = II, R4 = H).

IT **167407-71-8P 167407-86-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of amide-linked bis(DOTA) compds. as contrast agent chelants)

RN 167407-71-8 CAPLUS

CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10,10'-[(tetrahydro-1H-1,4-diazepine-1,4(5H)-diyl)bis(2-oxo-2,1-ethanediyl)]bis- (9CI) (CA INDEX NAME)

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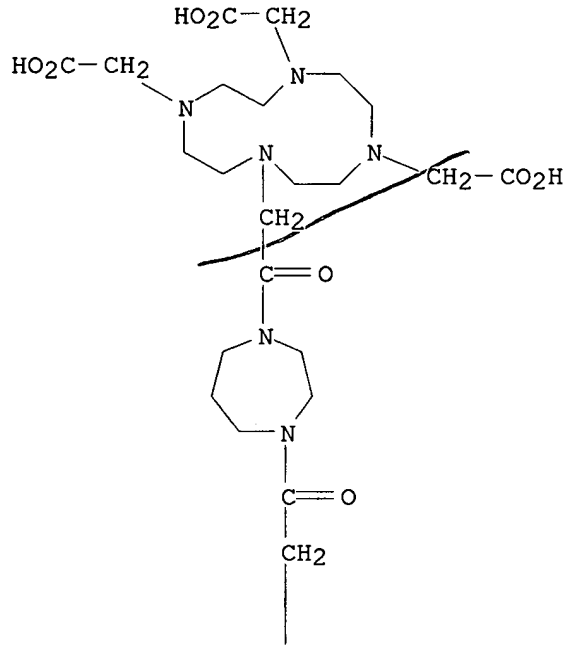

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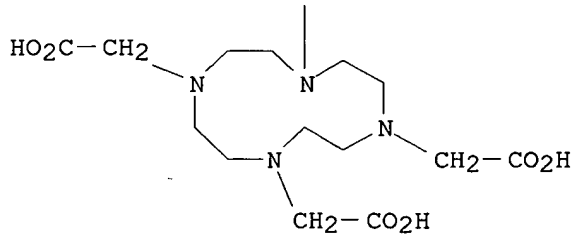

RN 167407-86-5 CAPLUS

CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10,10'-[(tetrahydro-1H-1,4-diazepine-1,4(5H)-diyl)bis(2-oxo-2,1-ethanediyl)]bis-, hexakis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

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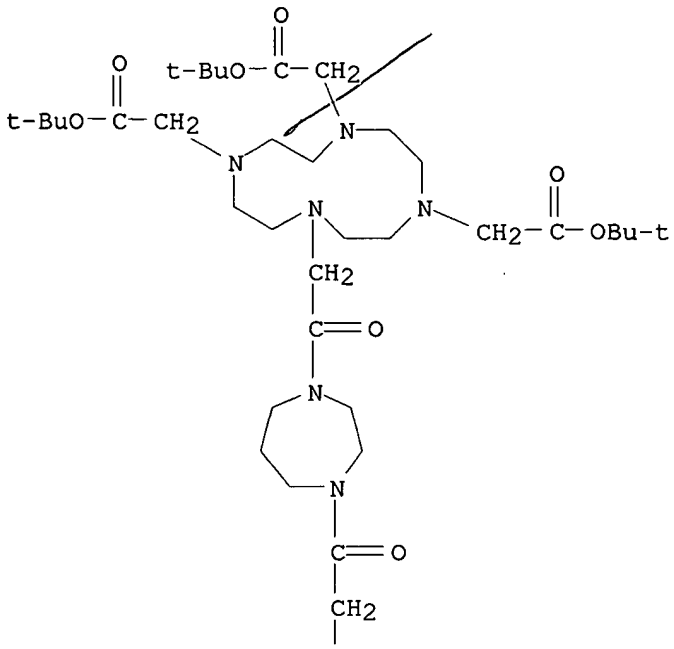

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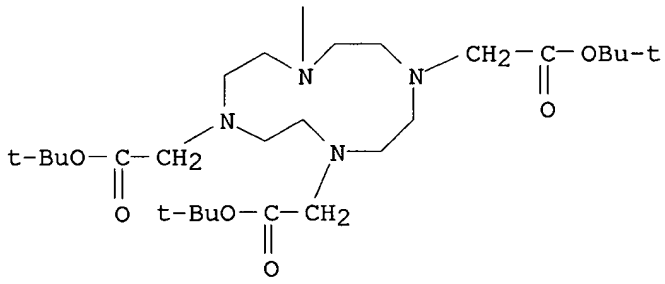


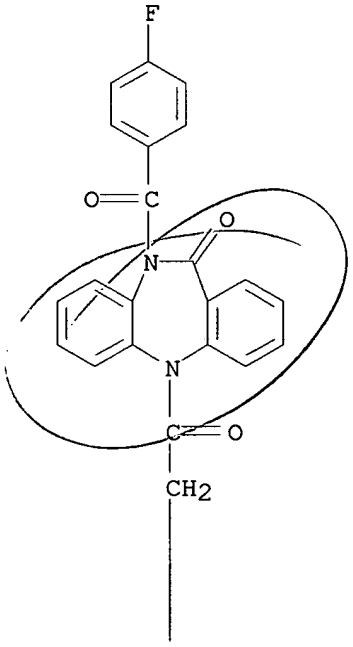
L5 ANSWER 26 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1997:285637 CAPLUS
DOCUMENT NUMBER: 126:343544
TITLE: Synthesis and evaluation of halogenated dibenzodiazepines as muscarinic receptor ligands
AUTHOR(S): Kassiou, Michael; Read, Roger W.; Shi, Xue-Qin
CORPORATE SOURCE: Radiopharmaceuticals Division, ANSTO, Menai, NSW 2234, Australia
SOURCE: Bioorganic & Medicinal Chemistry Letters (1997), 7(7), 799-804
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

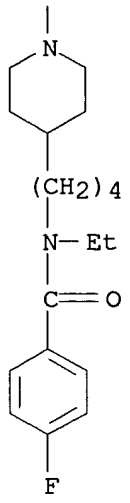
AB Syntheses of four novel amide analogs of the muscarinic M2 receptor antagonists, DIBA and BIBN 140, are described from a common intermediate. Pharmacol. evaluation through in vitro assays reveals high muscarinic receptor affinity in each of the compds., but variable subtype selectivity, primarily M2 but in one case M3.

IT **189938-94-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. and muscarinic receptor binding of dibenzodiazepines)

RN 189938-94-1 CAPLUS
CN Benzamide, N-ethyl-4-fluoro-N-[4-[1-[2-[10-(4-fluorobenzoyl)-10,11-dihydro-11-oxo-5H-dibenzo[b,e][1,4]diazepin-5-yl]-2-oxoethyl]-4-piperidinyl]butyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

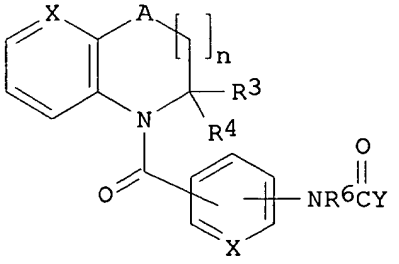



N
(CH2)4
N—Et
C=O
F

L5 ANSWER 27 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1995:807928 CAPLUS
DOCUMENT NUMBER: 123:198646
TITLE: Benzamide derivatives and their use as vasopressin antagonists
INVENTOR(S): Setoi, Hiroyuki; Ohkawa, Takehiko; Zenkoh, Tatsuya; Hemmi, Keiji; Tanaka, Horokazu
PATENT ASSIGNEE(S): Fujisawa Pharmaceutical Co., Ltd., Japan
SOURCE: Eur. Pat. Appl., 110 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 620216	A1	19941019	EP 1994-105344	19940407
EP 620216	B1	20030108		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
US 5521170	A	19960528	US 1994-220695	19940331
AT 230729	E	20030115	AT 1994-105344	19940407
ES 2185635	T3	20030501	ES 1994-105344	19940407
AU 9459322	A1	19941020	AU 1994-59322	19940408
AU 679719	B2	19970710		
CA 2121112	AA	19941014	CA 1994-2121112	19940412
JP 07002800	A2	19950106	JP 1994-72997	19940412
CN 1098406	A	19950208	CN 1994-103577	19940412
CN 1058710	B	20001122		
HU 70197	A2	19950928	HU 1994-1041	19940412
ZA 9402325	A	19950216	ZA 1994-2325	19941031

PRIORITY APPLN. INFO.: GB 1993-7527 A 19930413
OTHER SOURCE(S): MARPAT 123:198646
GI



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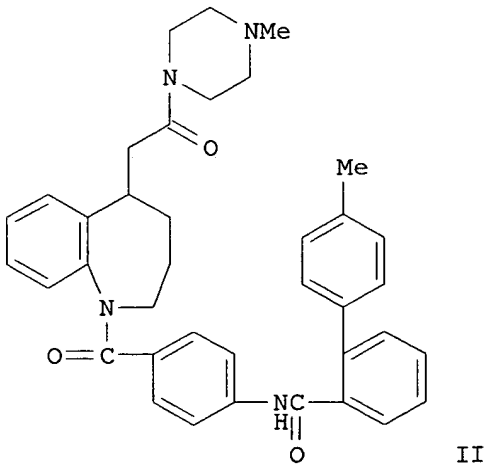

II

AB Benzamide derivs. I (R1 = H, alkyl, etc.; R2 = H, alkyl, haloalkyl, etc.;

R3, R4 = H, alkyl, etc.; R3R4 taken together form oxo; R5 = H, halo, nitro, hydroxy, etc.; R6 = H, alkyl, acyl; A = aminomethylene, alkanediyl, alkenediyl, etc.; X, Y = nitrogen, methine; n = integer) were disclosed as vasopressin antagonists. I are useful for the treatment or prevention of hypertension, heart failure renal insufficiency, edema, ascites, vasopressin parasecretion syndrome, hepatocirrhosis, hyponatremia, hypokalemia, diabetic and circulation disorders. An example compd., 1-[4-[2-(4-methylphenyl)benzoylamino]benzoyl]-5-[[(4-methyl-1-piperazinyl)carbonyl]methyl]-2,3,4,5-tetrahydro-1H-1-benzazepine (II) was prepd. in several steps.

IT **168046-23-9P**

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of benzamide derivs. vasopressin antagonists)

RN 168046-23-9 CAPLUS

CN [1,1'-Biphenyl]-2-carboxamide, N,N'-[(3,4-dihydro-1H-1,5-benzodiazepine-1,5(2H)-diyl)bis(carbonyl-4,1-phenylene)]bis[4'-methyl- (9CI) (CA INDEX NAME)

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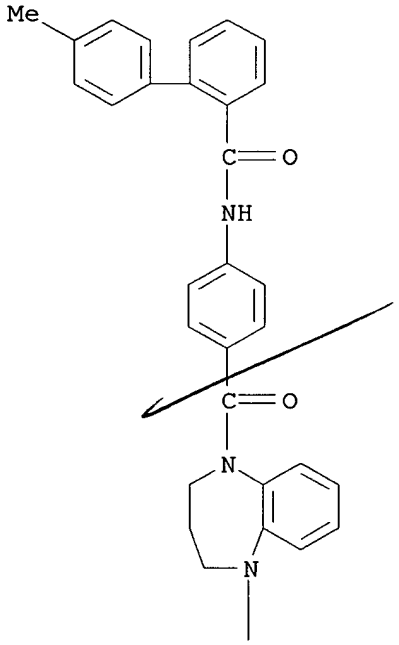
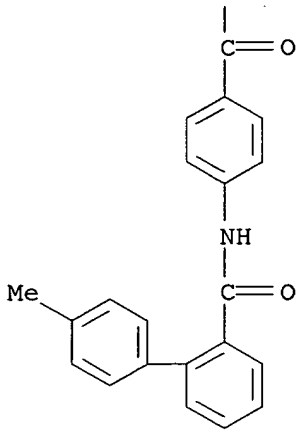


PAGE 2-A

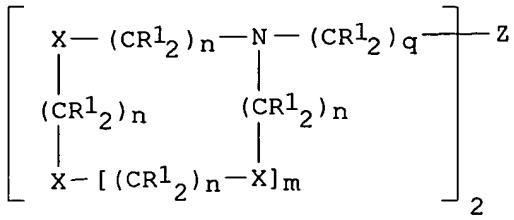


L5 ANSWER 28 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1995:780306 CAPLUS
DOCUMENT NUMBER: 123:186921
TITLE: Polyazacycloalkanes as dichelants
INVENTOR(S): Carvalho, Joan; Fellmann, Jere Douglas; Watson, Alan David; Koo, Michael
PATENT ASSIGNEE(S): Nycomed Salutar, Inc., USA; Cockbain, Julian Roderic Michaelson
SOURCE: PCT Int. Appl., 75 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9509848	A2	19950413	WO 1994-GB2115	19940929
WO 9509848	A3	19950727		
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, US				
RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5281704	A	19940125	US 1990-468107	19900119
JP 2000136174	A2	20000516	JP 1999-192219	19901020
US 5446145	A	19950829	US 1993-86996	19930707
CA 2172735	AA	19950413	CA 1994-2172735	19940929
AU 9477042	A1	19950501	AU 1994-77042	19940929
AU 678603	B2	19970605		
EP 722442	A1	19960724	EP 1994-927742	19940929
EP 722442	B1	20030115		
R: DE, DK, ES, FR, IE, IT				
CN 1136313	A	19961120	CN 1994-194300	19940929
CN 1045772	B	19991020		
HU 74592	A2	19970128	HU 1996-805	19940929
JP 09503500	T2	19970408	JP 1994-510671	19940929

PRIORITY APPLN. INFO.:
US 1990-468107 A2 19900119
US 1992-855028 A2 19920612
US 1993-86996 A2 19930707
GB 1993-20277 A 19931001
GB 1989-23843 A 19891023
JP 1990-515144 A3 19901020
WO 1994-GB2115 W 19940929

OTHER SOURCE(S): MARPAT 123:186921
GI



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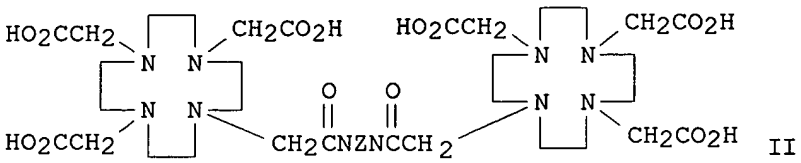

II

AB I (X same or different NZ, O or S, at least two Xs being NZ; each Z is a group R1 or a group CR12Y, at least one Z, and preferably 2 or 3 Zs, on each macrocyclic ring being a group CR12Y; each Y is a group CO2H, PO3H, SO3H, CONR12, CON(OR1)R1, CNS or CONR1NR12, preferably COOH; m is 0 or 1 or 2, preferably 1; each n is 2 or 3, preferably 2; q is 1 or 2, preferably 1; each R1 which may be the same or different is a H atom or an alkyl group optionally substituted by one or more hydroxy and/or alkoxy groups; and D is a bridging group, other than an unsubstituted carbonylaminoethylaminocarbonyl group, having a mol. wt. of <1000, preferably <500, joining two macrocyclic rings via at least one amide or ester bond) and salts and metal chelates were prepd. Thus I (Z = org. radicals) and their Gd or Dy dinuclear complexes were prepd. The Gd complexes were tested a MRI imaging agents.

IT **167407-86-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(for prepn. of bis(tetraazacyclododecyl) derivs.)

RN 167407-86-5 CAPLUS

CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10,10'-[(tetrahydro-1H-1,4-diazepine-1,4(5H)-diyl)bis(2-oxo-2,1-ethanediyl)]bis-, hexakis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

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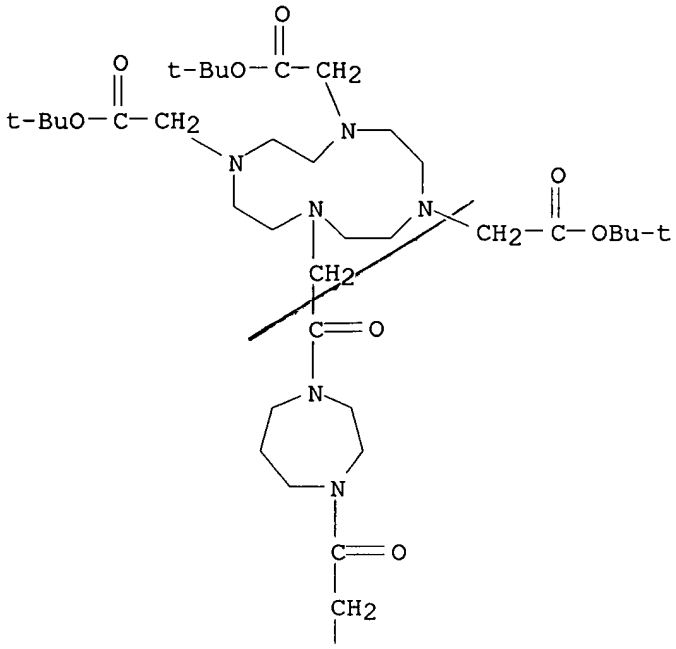

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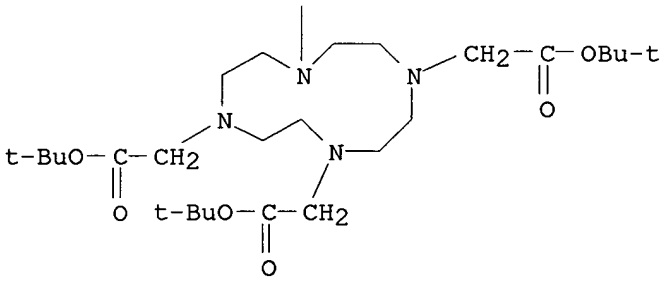
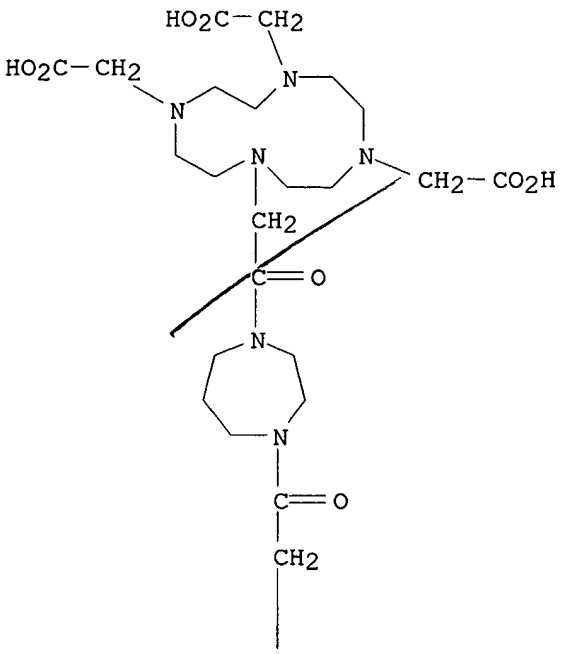


IT **167407-71-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and complexation with gadolinium)
RN 167407-71-8 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10,10'-[(tetrahydro-1H-1,4-diazepine-1,4(5H)-diyl)bis(2-oxo-2,1-ethanediyl)]bis- (9CI) (CA INDEX NAME)

PAGE 1-A



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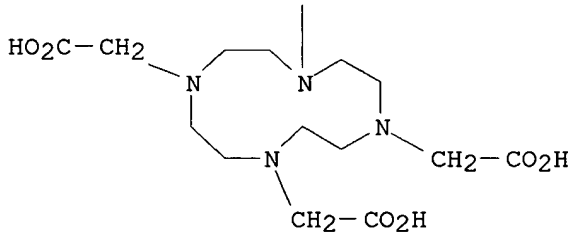
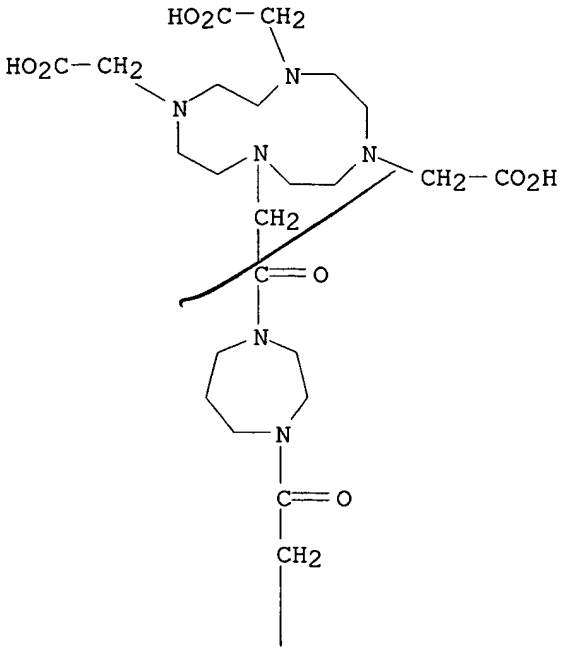


IT **167407-71-8DP**, gadolinium complex
RL: BUU (Biological use, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. and use as imaging agent)
RN 167407-71-8 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10,10'-[(tetrahydro-1H-1,4-diazepine-1,4(5H)-diyl)bis(2-oxo-2,1-ethanediyl)]bis- (9CI) (CA INDEX NAME)

PAGE 1-A



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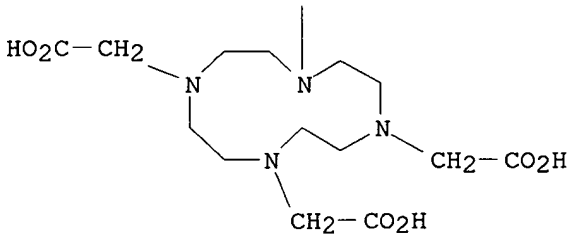
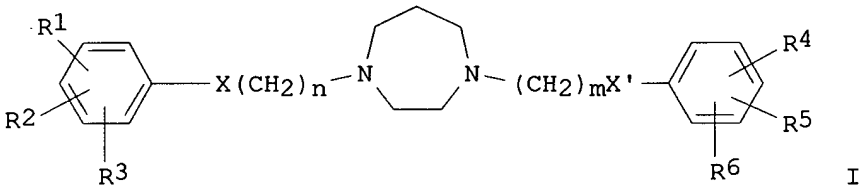


L5 ANSWER 29 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1995:767806 CAPLUS
DOCUMENT NUMBER: 123:179521
TITLE: Homopiperazines as cell migration inhibitors
INVENTOR(S): Kataoka, Kenichiro; Morita, Takuya; Ishii, Koji; Tanaka, Hiroko; Endo, Noriaki
PATENT ASSIGNEE(S): Teijin Ltd, Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 6 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 07145060	A2	19950606	JP 1993-295456	19931125

PRIORITY APPLN. INFO.: JP 1993-295456 19931125
OTHER SOURCE(S): MARPAT 123:179521
GI

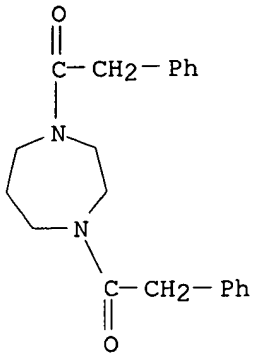


I

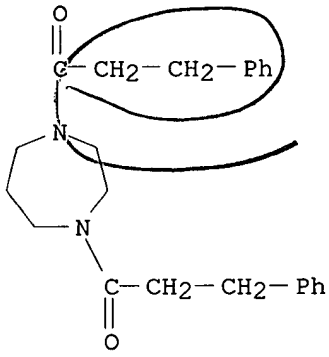
AB Inhibitors for chemokine-induced cell migration contain homopiperazines I [R1-6 = H, halo, OH, lower alkyl, lower alkoxy, lower acyloxy; X, X' = O, NH, NHCO, CONH, NHCONH, SO2NH.fwdarw., COS.fwdarw., CO2.fwdarw.; .fwdarw. = bond with (CH2)n or (CH2)m; n, m = 1-5] or their pharmacol. acceptable salts as active ingredients. The homopiperazines are useful for treatment of arteriosclerosis, rheumatoid arthritis, osteoarthritis, diabetic retinopathy, pulmonary fibrosis, etc. N,N'-bis(phenylacetyl)homopiperazine (336 mg) was stirred with LiAlH4 in dry ether at room temp. for 3 days to give 150 mg N,N'-bis(2-phenylethyl)homopiperazine (II), which was converted to II.2HCl (III). III inhibited the migration of human leukemia cells THP-1, induced by MCP-1 (monocyte chemotactic protein-1), with IC50 of 400 .mu.M. Formulations of tablets and injections are given.

IT **167636-47-7P 167636-48-8P 167636-49-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(homopiperazines as chemokine-induced cell migration inhibitors for therapeutic use)

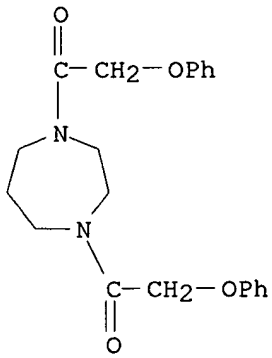
RN 167636-47-7 CAPLUS
CN 1H-1,4-Diazepine, hexahydro-1,4-bis(phenylacetyl)- (9CI) (CA INDEX NAME)



RN 167636-48-8 CAPLUS
CN 1H-1,4-Diazepine, hexahydro-1,4-bis(1-oxo-3-phenylpropyl)- (9CI) (CA INDEX NAME)



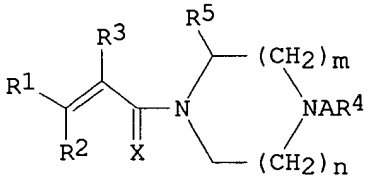
RN 167636-49-9 CAPLUS
CN 1H-1,4-Diazepine, hexahydro-1,4-bis(phenoxyacetyl)- (9CI) (CA INDEX NAME)



L5 ANSWER 30 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1994:54554 CAPLUS
DOCUMENT NUMBER: 120:54554
TITLE: Preparation of N-(3,3-disubstituted acryloyl)piperazines as PAF antagonists
INVENTOR(S): Nakamura, Norio; Ookawa, Nobuyuki; Ooshima, Takeshi; Myamoto, Masaaki; Iijima, Yasuteru
PATENT ASSIGNEE(S): Sankyo Co, Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 107 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 05097819	A2	19930420	JP 1991-170853	19910711
JP 3058945	B2	20000704		

PRIORITY APPLN. INFO.: JP 1990-289474 A1 19901026
OTHER SOURCE(S): MARPAT 120:54554
GI



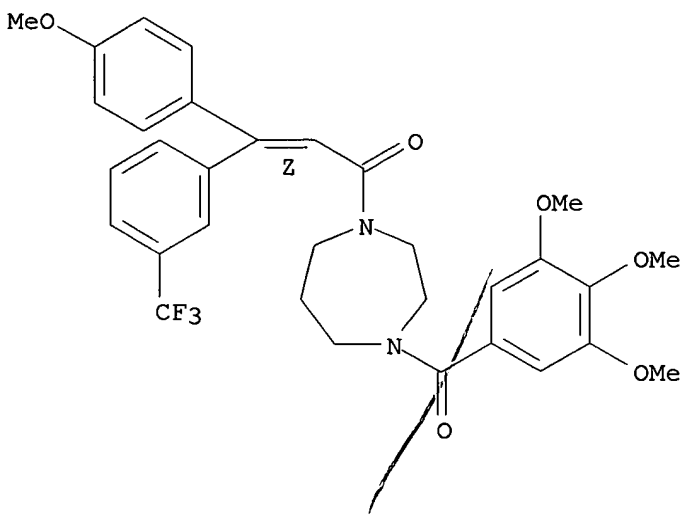
I

AB The title compds. [I; R1, R2 = -CH:CH-R6, C.tplbond.C-R6, etc.; R6 = (un)substituted aryl, (un)substituted heteroaryl; R3 = H, alkyl, cyano, groups contg. R6; R4 = (un)substituted phenyl, etc.; R5 = H, alkyl; or R3R5 = (CH2)p; p = 1-3 integer; X = O, S; A = alkylene, CO, CS, SO, SO2; m, n = 1, 2], PAF antagonists and therefore useful for treatment of many cardiovascular diseases, e.g., hypertension, are prepd. 3-Phenylcinnamic acid in CH2Cl2 contg. PCl5 was stirred at room temp. for 1 h to give the acid chloride, which was reacted with 1-(3,4,5-trimethoxybenzoyl)piperazine in THF at room temp. for 30 min to give 1-(3-phenylcinnamoyl)-4-(3,4,5-trimethoxybenzoyl)piperazine. In an in vitro study, this had an IC50 of 3.2.times.10-7 M against PAF blood platelet aggregation. Pharmaceutical compns. contg. I are described.

IT **151664-78-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of, as cardiovascular agent)

RN 151664-78-7 CAPLUS
CN 1H-1,4-Diazepine, hexahydro-1-[3-(4-methoxyphenyl)-1-oxo-3-[3-(trifluoromethyl)phenyl]-2-propenyl]-4-(3,4,5-trimethoxybenzoyl)-, (Z)-(9CI) (CA INDEX NAME)

Double bond geometry as shown.


MeO
Z
O
N
N
OMe
OMe
OMe
CF3
O

L5 ANSWER 31 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1992:33204 CAPLUS
DOCUMENT NUMBER: 116:33204
TITLE: New conformationally restricted technetium-99m N2S2 complexes as myocardial perfusion imaging agents
AUTHOR(S): Ohmomo, Yoshiro; Francesconi, Lynn; Kung, Mei Ping; Kung, Hank F.
CORPORATE SOURCE: Dep. Radiol., Univ. Pennsylvania, Philadelphia, PA, 19104, USA
SOURCE: Journal of Medicinal Chemistry (1992), 35(1), 157-62
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
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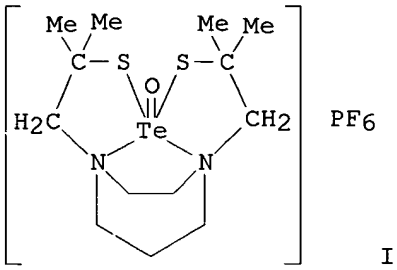


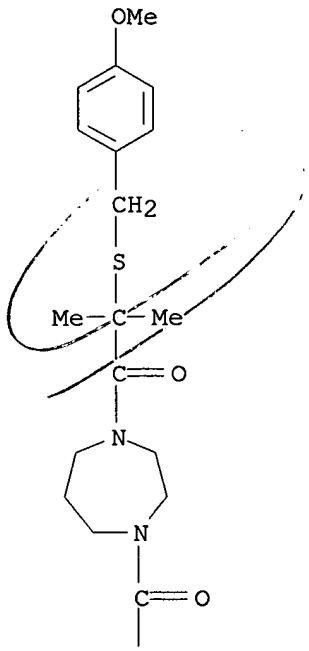
I

AB In developing 99mTc complexes as potential myocardial imaging agents, a new series of ligands based on a conformationally restricted N2S2 system were investigated. Using piperazine or homopiperazine as the starting material, two N2S2 ligands with addnl. conformation restriction between the two N donor atoms were synthesized. The 99mTc complexes were prepd. by a direct labeling method with Sn(II) as the reducing agent for [99mTc]-pertechnetate. The resulting, 99mTc complexes were purified through a sulfonpropyl Sephadex column and further purified by HPLC with a reverse-phase column eluting with a solvent system of MeCN/buffer. Biodistribution studies in rats showed initial uptake in the heart (0.21%, 0.42% dose/organ for the 99Tc-labeled complexes with the piperazine- and homopiperazine-based ligands pertechnetate. The resulting 99mTc complexes were purified through a sulfonpropyl Sephadex column and further purified by HPLC with a reverse-phase column eluting with a solvent system of MeCN/buffer. Biodistribution studies in rats showed initial uptake in the heart (0.21%, 0.42% dose/organ for the 99Tc-labeled complexes with the piperazine-homopiperazine-based ligands at 2 min post-injection). Carrier-added prepn. of I was successful. NMR, IR, UV, crystallog., and elemental anal. of IPF6 suggest that this series of 1+ charged 99mTc complexes may have potential as myocardial imaging agents, and further study of the complexes is warranted. Crystal data for I: monoclinic P21/n, Z = 4, R1 = 0.056, R2 = 0.061.

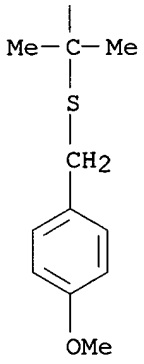
IT **136847-18-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and redn. of, by borane)

RN 136847-18-2 CAPLUS
CN 1H-1,4-Diazepine, hexahydro-1,4-bis[2-[[(4-methoxyphenyl)methyl]thio]-2-methyl-1-oxopropyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A



ES ANSWER 32 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1992:20955 CAPLUS
DOCUMENT NUMBER: 116:20955
TITLE: Preparation of isoquinoline-5-sulfonamides and analogs as blood vessel relaxants
INVENTOR(S): Hidaka, Hiroyoshi; Ishikawa, Tomohiko; Hagiwara, Masatoshi; Inoue, Tsutomu; Naitoh, Kenji; Sakuma, Osamu; Yuasa, Masayuki; Morita, Tadashi; Toshioka, Tadashi; et al.
PATENT ASSIGNEE(S): Tobishi Pharmaceutical Co., Ltd., Japan
SOURCE: Ger. Offen., 86 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

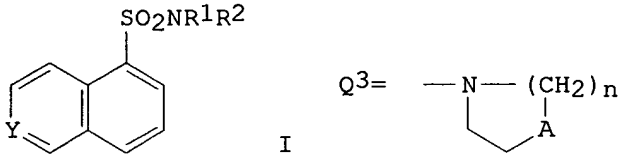
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3942114	A1	19900628	DE 1989-3942114	19891220
DE 3942114	C2	19970904		
CA 2005741	AA	19900626	CA 1989-2005741	19891215
CA 2005741	C	19980602		
JP 02256666	A2	19901017	JP 1989-325959	19891218
JP 2886225	B2	19990426		
SE 8904261	A	19900627	SE 1989-4261	19891219
SE 503081	C2	19960318		
US 5081246	A	19920114	US 1989-453623	19891220
DE 3943678	C2	19991125	DE 1989-3943678	19891220
GB 2228933	A1	19900912	GB 1989-28895	19891221
GB 2228933	B2	19930331		
CH 680441	A	19920831	CH 1989-4647	19891221
DK 8906662	A	19900627	DK 1989-6662	19891222
FR 2640973	A1	19900629	FR 1989-17091	19891222
FR 2640973	B1	19920327		
NL 8903143	A	19900716	NL 1989-3143	19891222
NL 193726	B	20000403		
NL 193726	C	20000804		
ES 2029759	A6	19920901	ES 1989-4335	19891222
AT 8902935	A	19940215	AT 1989-2935	19891222
CN 1044098	A	19900725	CN 1989-109843	19891226
CN 1025618	B	19940810		
JP 03007262	A2	19910114	JP 1990-11719	19900123
JP 3048590	B2	20000605		
JP 03047170	A2	19910228	JP 1990-52686	19900306
JP 3078295	B2	20000821		
US 5216150	A	19930601	US 1991-758808	19910912
GB 2248235	A1	19920401	GB 1991-22595	19911024
GB 2248235	B2	19930331		
US 5245034	A	19930914	US 1992-856178	19920323
CN 1074214	A	19930714	CN 1992-115101	19921230
CN 1028638	B	19950531		
NL 9900004	A	19990901	NL 1999-4	19990517
NL 194549	B	20020301		
NL 194549	C	20020702		

PRIORITY APPLN. INFO.: JP 1988-325910 A 19881226
JP 1989-76419 A 19890330
JP 1989-87868 A 19890410

DE 1989-3942114	A3	19891220
US 1989-453623	A3	19891220
GB 1989-28895	A3	19891221
NL 1989-3143	A3	19891222
CN 1989-109843	A	19891226
US 1991-758808	A3	19910912

OTHER SOURCE(S): MARPAT 116:20955

GI



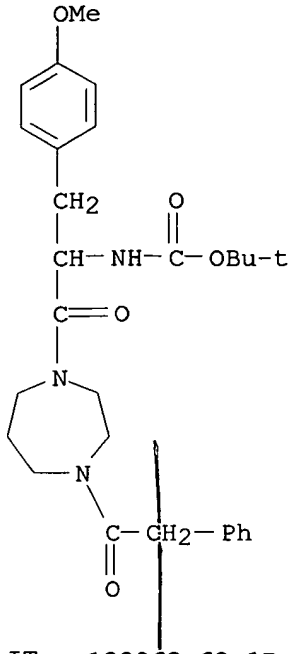
I

AB The title compds. [I; R1 = H, CHO, (halophenyl)propargyl, (un)substituted alkyl, aralkyl, Ph; R2 = WNR3CHR4XmQ1, CH(CR12R13R)CH2Q2, W = alkylene, (un)substituted phenylenediyl, or a combination of these; R3 = R1; R1R3 = alkylene; R4 = H, alkyl; X = CH:CH, C.tplbond.C; Q1, Q2 = (un)substituted Ph, naphthyl, heterocyclyl; R12, R13 = H; R12R13 = O; R = Q3; A = CO, (un)substituted CH2, NH, etc.; R1R3 = alkylene; Y = N, CH, CMe; m, n = 1-3] were prepd. Thus, I (R1 = H, Y = N) (II; R2 = CH2CH2NH2) was stirred 1 h with 4-ClC6H4CH:CHCHO in MeOH after which NaBH4 was added and stirring continued 30 min to give II (R2 = CH2CH2NR5CH2CH:CHC6H4Cl-4) (III; R5 = H) which was methylated to give III (R5 = Me). The latter had EC50 of 0.19 .mu.M for relaxation of rabbit aorta strips in vitro.

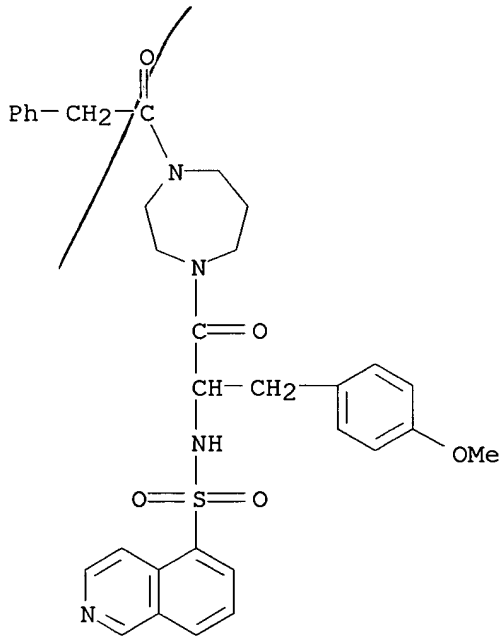
IT **130963-60-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and reaction of, in prepn. of blood vessel relaxants)

RN 130963-60-9 CAPLUS

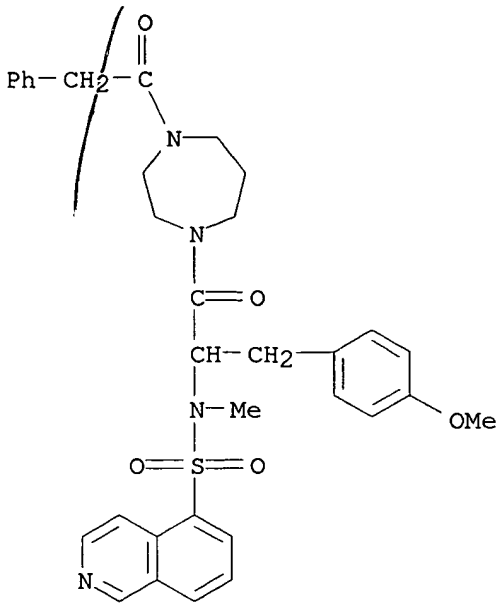
CN Carbamic acid, [2-[hexahydro-4-(phenylacetyl)-1H-1,4-diazepin-1-yl]-1-[(4-methoxyphenyl)methyl]-2-oxoethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



IT **130963-62-1P 130963-63-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as blood vessel relaxant)
RN 130963-62-1 CAPLUS
CN 1H-1,4-Diazepine, hexahydro-1-[2-[(5-isoquinolinylsulfonyl)amino]-3-(4-methoxyphenyl)-1-oxopropyl]-4-(phenylacetyl)- (9CI) (CA INDEX NAME)



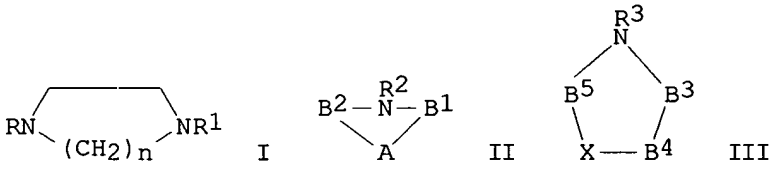
RN 130963-63-2 CAPLUS
CN 1H-1,4-Diazepine, hexahydro-1-[2-[(5-isoquinolinylsulfonyl)methylamino]-3-(4-methoxyphenyl)-1-oxopropyl]-4-(phenylacetyl)- (9CI) (CA INDEX NAME)

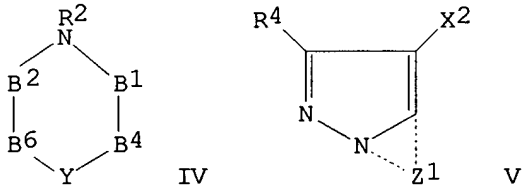


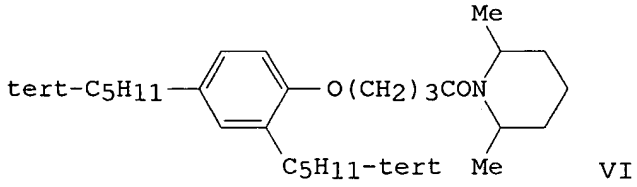
L5 ANSWER 33 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1991:460742 CAPLUS
DOCUMENT NUMBER: 115:60742
TITLE: Silver halide color photographic material containing nitrogen heterocycles
INVENTOR(S): Morigaki, Masakazu; Seto, Nobuo
PATENT ASSIGNEE(S): Fuji Photo Film Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 72 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 02262654	A2	19901025	JP 1989-316114	19891205
JP 2641070	B2	19970813		
US 5028519	A	19910702	US 1989-446313	19891205

PRIORITY APPLN. INFO.: JP 1988-308660 19881206
GI







AB The material contains .gtoreq.1 of the heterocycles I, II, III, IV, etc.[R,R1 = acyl, sulfonyl, sulfinyl, alkyloxycarbonyl, aryloxycarbonyl, phosphoryl, SO2NH2, CONH2; n = 1-3; R2,R3 = H, alkenyl, aryl group listed in R,R1; addnl. R3 = alkyl, heterocyclyl; B1,B2,B3,B4,B6 = (un)substituted CH2, CO; B5 = (un)substituted CH2; A = atoms to complete a 5- to 8-membered ring; X,Y = O, S, SO, SO2, (un)substituted NH] in any layer on a support and has .gtoreq.1 layer contg. a pyrazole-type magenta coupler [V; R4 = H, substituent; Z1 = nonmetal atoms to complete an (un)substituted or fused azole ring; X2 = H, leaving group]. I-IV improve

the storage stability of the yellow and cyan dye image against light and heat and prevent the formation of yellow stains in the white. A dye image obtained from a multilayer Ag halide photog. paper with a layer contg. a yellow coupler and a dye image stabilizer, e.g. VI, retained 87-96% of the yellow d. after exposing for 8 days to a xenon tester (200,000 lx illuminance) and 90-96% after heating 400 h at 100.degree..

IT **135122-54-2 135122-55-3**
RL: USES (Uses)
(silver halide color photog. material contg., for stabilization of yellow and cyan dye images)

RN 135122-54-2 CAPLUS

CN 1H-1,4-Diazepine, 1,4-bis[2-[2,4-bis(1,1-dimethylpropyl)phenoxy]-1-oxobutyl]hexahydro- (9CI) (CA INDEX NAME)

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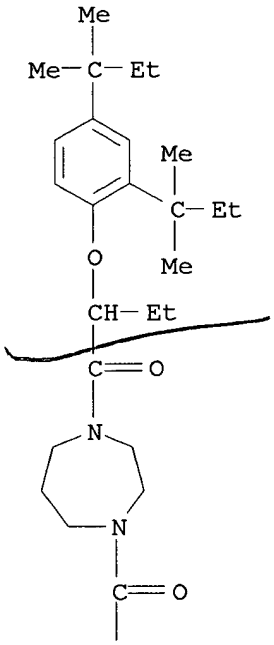
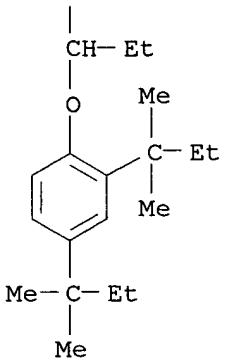
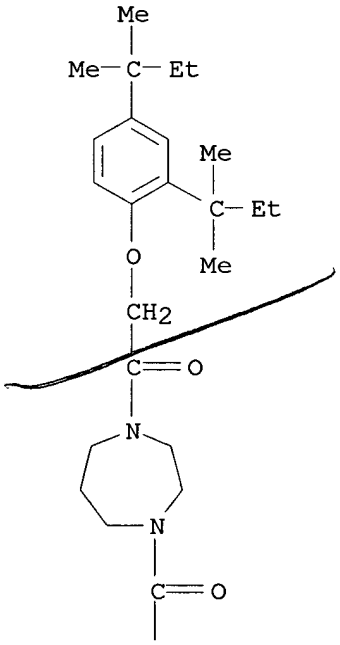


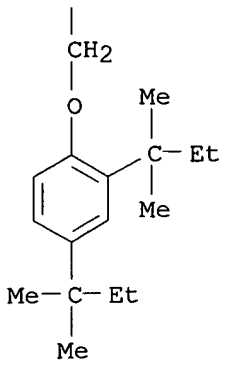
PAGE 2-A



RN 135122-55-3 CAPLUS
CN 1H-1,4-Diazepine, 1,4-bis[[2,4-bis(1,1-dimethylpropyl)phenoxy]acetyl]hexahydro- (9CI) (CA INDEX NAME)

PAGE 1-A

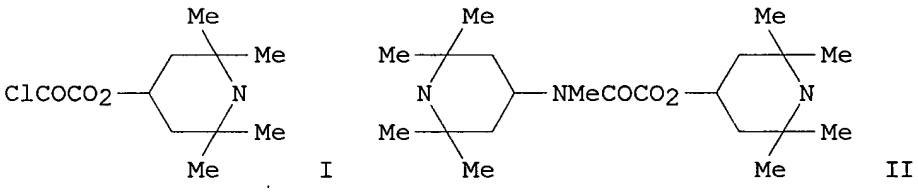



CH2
O
Me
C— Et
Me
Me— C— Et
Me

L5 ANSWER 34 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1988:21720 CAPLUS
DOCUMENT NUMBER: 108:21720
TITLE: Preparation of 2,2,6,6-tetramethylpiperidine derivatives as polymer stabilizers
INVENTOR(S): Cantatore, Giuseppe; Borzatta, Valerio
PATENT ASSIGNEE(S): Ciba-Geigy S.p.A., Italy
SOURCE: Ger. Offen., 45 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3613194	A1	19861023	DE 1986-3613194	19860418
GB 2174093	A1	19861029	GB 1986-9564	19860418
GB 2174093	B2	19880817		
CA 1261321	A1	19890926	CA 1986-507048	19860418
FR 2580639	A1	19861024	FR 1986-5688	19860421
FR 2580639	B1	19880520		
JP 61251660	A2	19861108	JP 1986-93201	19860422
US 4780493	A	19881025	US 1986-854742	19860422
US 4999392	A	19910312	US 1988-224028	19880721

PRIORITY APPLN. INFO.: IT 1985-20441 19850422
US 1986-854742 19860422
OTHER SOURCE(S): CASREACT 108:21720
GI



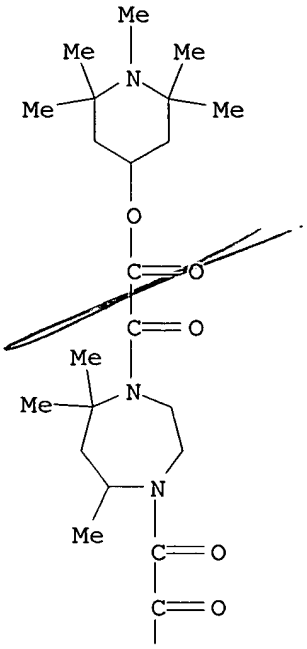
AB X(COCO2R1)m [R1 = C3-18 alkenyl, (un)substituted C1-18 alkyl, C5-18 cycloalkyl, C6-18 aryl, C7-18 aralkyl; X = polyfunctional (poly)amine residue incorporating tetramethylpiperidine residue(s)], were prepd. as light stabilizers for polymers. Thus, 51.1 g 2,2,6,6-tetramethyl-4-piperidinol.HCl was esterified with (COCl)2 to give 73.5 g chlorocarbonylacetate I HCl. The latter (28.4 g) and 20.4 g 4-(methylamino)-2,2,6,6-tetramethylpiperidine were stirred in CH2Cl2 1 h at 0-5.degree. and 4 h at room temp. to give 28.5 g piperidinyloxamate II. In polypropylene contg. phthalocyanine blue 0.1% II delayed onset of light-induced chalking for 2700 h, compared to 510 h for the control.

IT **111989-30-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as light stabilizer for plastics)

RN 111989-30-1 CAPLUS

CN 1H-1,4-Diazepine-1,4(5H)-diacetic acid, tetrahydro-5,5,7-trimethyl-.alpha.,.alpha.'-dioxo-, bis(1,2,2,6,6-pentamethyl-4-piperidinyl) ester (9CI) (CA INDEX NAME)

PAGE 1-A



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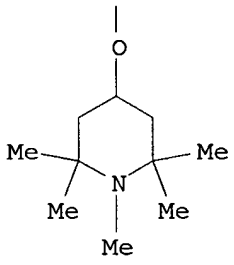
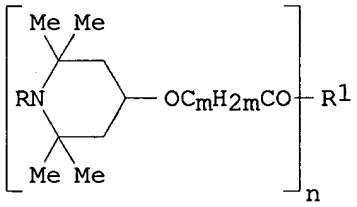


L5 ANSWER 35 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1986:110770 CAPLUS
DOCUMENT NUMBER: 104:110770
TITLE: Compounds containing piperidine rings and their use in the stabilization of synthetic polymers
INVENTOR(S): Cantatore, Giuseppe; Borzatta, Valerio
PATENT ASSIGNEE(S): Ciba-Geigy S.p.A., Italy
SOURCE: Eur. Pat. Appl., 28 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 153907	A2	19850904	EP 1985-810074	19850222
EP 153907	A3	19870513		
EP 153907	B1	19921111		
R: BE, DE, FR, GB, IT				
CA 1236098	A1	19880503	CA 1985-475147	19850226
US 4618634	A	19861021	US 1985-706301	19850227
JP 60202860	A2	19851014	JP 1985-40274	19850228
JP 05082384	B4	19931118		

PRIORITY APPLN. INFO.: IT 1984-19830 19840228
GI



I

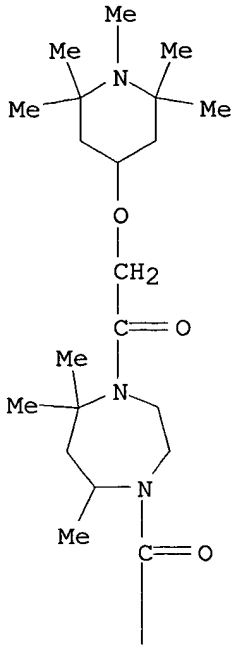
AB Synthetic polymers can be stabilized by the addn. of piperidine-contg. compds. (I), where R is H, O, CH2CN, C1-12 alkyl, C3-12 alkenyl or alkynyl, or C1-12 acyl, m is 1-12, n is 1-3, and R1 is an amine residue. For example, a stabilizer was prepd. by mixing 38.9 g N,N'-bis(2-chloroacetyl)-N,N'-bis(2,2,6,6-tetramethylpiperidin-4-yl)-1,6-diaminohexane in 100 mL anhyd. xylene with the Na salt of 26.38 g 1,2,2,6,6-pentamethylpiperidin-4-ol in 120 mL anhyd. xylene. A mixt. of the stabilizer 2, pentaerythritol tetrakis[3-(3,5-di-tert-butyl-4-hydroxyphenyl)propionate] (antioxidant) 1, polypropylene (melt index 2.4) 1000, and Co stearate 1 g was extruded to form 50 .mu. .times. 2.5 mm bands, which required 2600 h in a weatherometer (63.degree.) for the tensile strength of the sample to be reduced 50%.

IT **100904-02-7P 100920-80-7P**
RL: PREP (Preparation)
(prepn. of, as stabilizer for polyolefins)

RN 100904-02-7 CAPLUS

CN 1H-1,4-Diazepine, hexahydro-5,5,7-trimethyl-1,4-bis[[(1,2,2,6,6-pentamethyl-4-piperidinyl)oxy]acetyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



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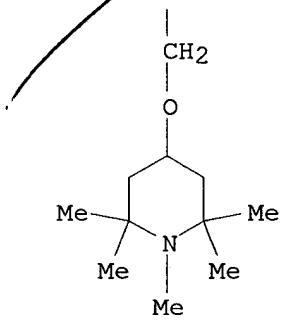
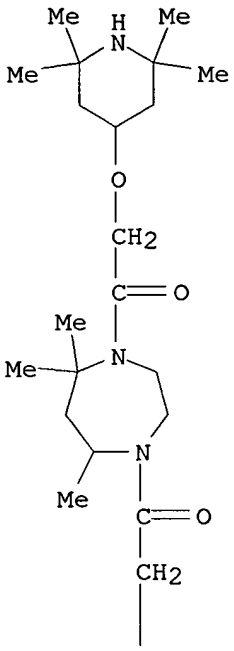


RN 100920-80-7 CAPLUS
CN 1H-1,4-Diazepine, hexahydro-5,5,7-trimethyl-1,4-bis[[(2,2,6,6-tetramethyl-4-piperidinyl)oxy]acetyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



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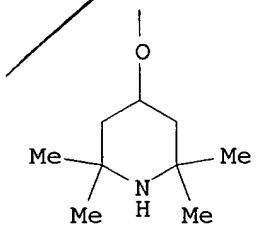
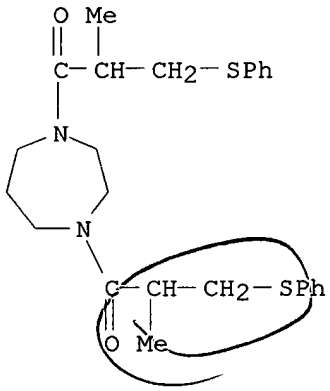


L5 ANSWER 36 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1985:560930 CAPLUS
DOCUMENT NUMBER: 103:160930
TITLE: Synthesis of poly(diketamide sulfides) containing a piperazine group in main chain
AUTHOR(S): Sugiyama, Kazuo
CORPORATE SOURCE: Coll. Eng., Kinki Univ., Kure, Japan
SOURCE: Kinki Daigaku Kogakubu Kenkyu Hokoku (1984), 18, 19-26
CODEN: KDKHD3; ISSN: 0386-491X
DOCUMENT TYPE: Journal
LANGUAGE: Japanese

AB N,N'-Dimethacryloylpiperazine (I) [17308-56-4] and N,N'-dimethacryloylhomopiperazine (II) [98755-64-7] here prepd. and polymd. with p-HSC8H4C6H4SH-p (III), CH2(C6H4SH-p)2 (IV), or p-HSC6H4CH2CH2C6H4SH-p (V). In DMSO at room temp., the polymn. of I or II with V proceeded sufficiently in the absence of a catalyst, while the polymn. was very fast in the presence of KF, LiCl, or triethylamine [108-98-5], with the triethylamine being most effective. In the polymn. of I or II with III in the presence of LiCl in a solvent at room temp., the conversion was in the order of CMSO > hempa > DMF. In the polymn. in the presence of LiCl in DMSO at room temp., the conversion has in the order of V > IV > III.

IT **98790-98-8**
RL: USES (Uses)
(model compd., for polyketamide-polysulfides)
RN 98790-98-8 CAPLUS
CN 1H-1,4-Diazepine, hexahydro-1,4-bis[2-methyl-1-oxo-3-(phenylthio)propyl]- (9CI) (CA INDEX NAME)



IT **98755-38-5P 98755-39-6P 98755-40-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 98755-38-5 CAPLUS
CN Poly[(tetrahydro-1H-1,4-diazepine-1,4(5H)-diyl)(2-methyl-1-oxo-1,3-propanediyl)thio-1,4-phenylene-1,2-ethanediyl-1,4-phenylenethio(2-methyl-3-oxo-1,3-propanediyl)] (9CI) (CA INDEX NAME)

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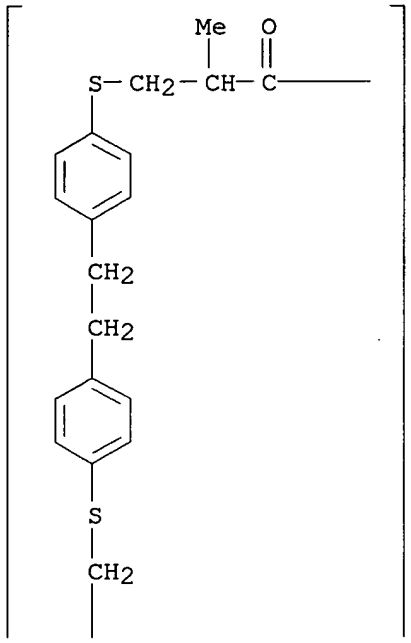

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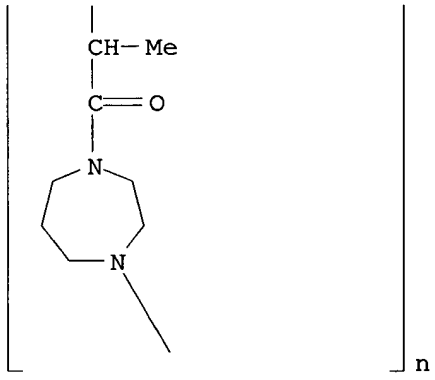
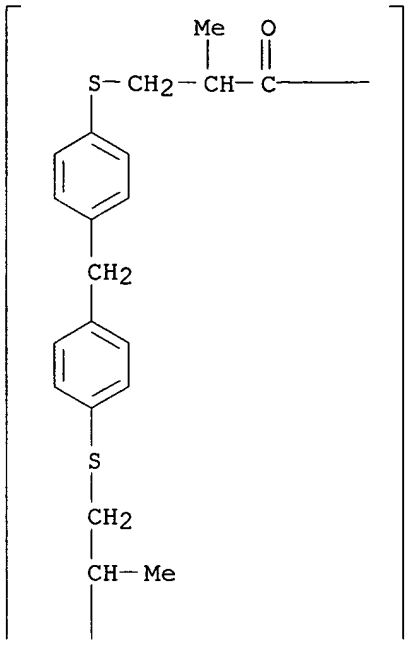
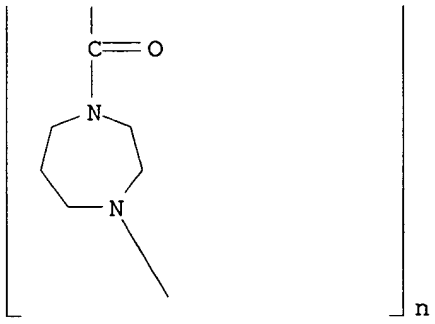


RN 98755-39-6 CAPLUS
CN Poly[(tetrahydro-1H-1,4-diazepine-1,4(5H)-diyl)(2-methyl-1-oxo-1,3-propanediyl)thio-1,4-phenylenemethylene-1,4-phenylenethio(2-methyl-3-oxo-1,3-propanediyl)] (9CI) (CA INDEX NAME)

PAGE 1-A

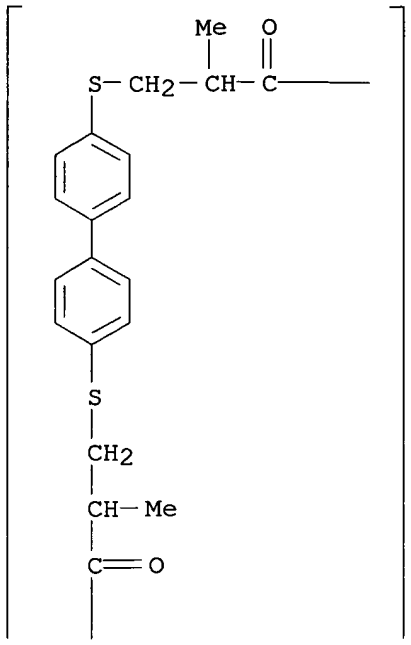


PAGE 2-A



RN 98755-40-9 CAPLUS
CN Poly[(tetrahydro-1H-1,4-diazepine-1,4(5H)-diyl)(2-methyl-1-oxo-1,3-propanediyl)thio[1,1'-biphenyl]-4,4'-diylthio(2-methyl-3-oxo-1,3-propanediyl)] (9CI) (CA INDEX NAME)

PAGE 1-A



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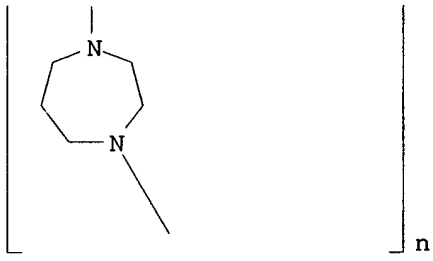
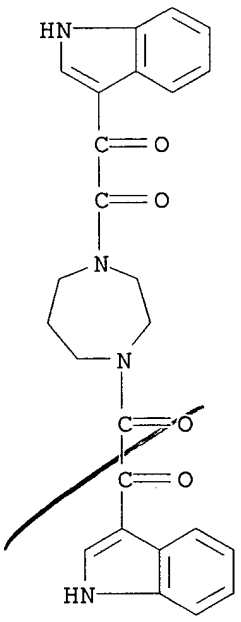


L5 ANSWER 37 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1979:568360 CAPLUS
DOCUMENT NUMBER: 91:168360
TITLE: Pharmacological evaluation of some newer piperidyl ethyl indoles as anti-parkinsonian agent
AUTHOR(S): Agarwal, Jagdish C.; Nath, C.; Sharma, M.; Kishor, K.; Shanker, K.; Gupta, G. P.; Bhargava, K. P.
CORPORATE SOURCE: Dep. Pharmacol. Ther., King George's Med. Coll., Lucknow, India
SOURCE: Indian Drugs (1979), 16(9), 209-12
CODEN: INDRBA; ISSN: 0019-462X
DOCUMENT TYPE: Journal
LANGUAGE: English

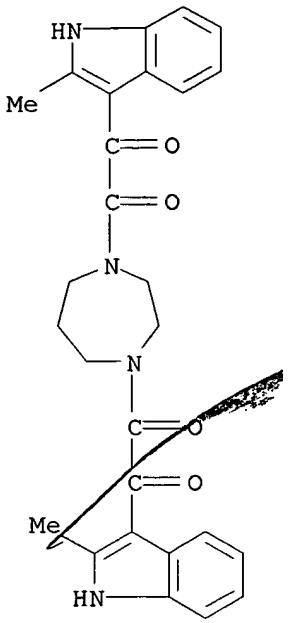
AB The antiparkinsonian and analgesic activities and the effects on locomotor activities of 23 indole derivs. were studied in rats and mice, and among these, 4 compds. antagonized oxotremorine-induced tremors, 10 antagonized reserpine-induced rigidity, and 1 decreased the locomotor activity, while 2 increased it. Only 2 compds. showed mild analgesic activity.

IT **22547-36-0 71765-64-5**
RL: BIOL (Biological study)
(as antiparkinsonian drug)

RN 22547-36-0 CAPLUS
CN 1H-1,4-Diazepine, hexahydro-1,4-bis(1H-indol-3-yloxoacetyl)- (9CI) (CA INDEX NAME)



RN 71765-64-5 CAPLUS
CN 1H-1,4-Diazepine, hexahydro-1,4-bis[(2-methyl-1H-indol-3-yl)oxoacetyl]- (9CI) (CA INDEX NAME)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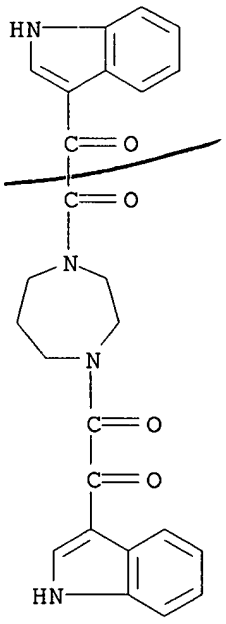
L5 ANSWER 38 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1974:563221 CAPLUS
DOCUMENT NUMBER: 81:163221
TITLE: 1,4-Bis(2-indol-3-ylethyl)piperazines
AUTHOR(S): Archibald, John L.; Freed, Meier E.
CORPORATE SOURCE: Res. Div., Wyeth Lab. Inc., Radnor, PA, USA
SOURCE: Journal of Medicinal Chemistry (1974), 17(7), 745-7
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A series of 17 title compds. were prepd. by the reaction of indoleglyoxoylchlorides with the appropriate piperazines, followed by LiAlH4 redn., or by dialkylation of the piperazines with indol-3-ylethyl halides. 1,4-Bis(2-indol-3-ylethyl)-cis-2,5-dimethylpiperazine (I) [52990-59-7] at 30 mg/kg. i.p. in rats caused >50 mm fall in systolic blood pressure 2 hr after dosing. 1,4-Bis[2-(2-methyl-3-indolyl)ethyl]piperazine (II) [22593-33-5] and 1,4-bis(2-indol-3-ylethyl)-2,6-dimethylpiperazine (III) [22547-42-8] caused marked antimorphine activity when administered orally to mice, with slight antihypertensive activity. 1,4-Bis[2-(1-methyl-3-indolyl)ethyl]piperazine (IV) [22540-25-6] and cis-2,5-dimethyl-1,4-bis[2-(1-methyl-3-indolyl)ethyl]piperazine (V) [52990-62-2] showed marked antitremorine activity in mice, with borderline antihypertensive activity. Structure-activity relations were discussed.

IT **22547-36-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 22547-36-0 CAPLUS
CN 1H-1,4-Diazepine, hexahydro-1,4-bis(1H-indol-3-yloxoacetyl)- (9CI) (CA INDEX NAME)



L5 ANSWER 39 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1969:115007 CAPLUS
DOCUMENT NUMBER: 70:115007
TITLE: Therapeutic bis(indolyl) compounds
PATENT ASSIGNEE(S): American Home Products Corp.
SOURCE: Brit., 23 pp.
CODEN: BRXXAA
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 1126245		19680905		

PRIORITY APPLN. INFO.: US 19651203

AB The title compds., tranquilizers, cardiovascular agents (e.g. antihypertensives), hypotensives, central nervous system depressants, anticonvulsants and analgesics, are prepd. Thus, to a stirred, refluxing mixt. of 2 g. 3-[2-(4-piperidyl)ethyl]indole (I), 1.9 g. Na2CO3, 0.32 ml. H2O, and 15 ml. iso-PrOH is added dropwise a soln. of 1.58 g. 3-(2-chloroethyl)indole in 4 ml. iso-PrOH, and the mixt. stirred 16 hrs. and worked up to give 3.2 g. 1,4-bis(2-indol-3-ylethyl)piperidine-HBr, m. 249-51.degree. (Me Cellosolve-H2O). 3-Indoleglyoxyloyl chloride (II) (16.8 g.) is added portionwise over 3 hrs. to a stirred mixt. of 20.56 g. 2-methyl-3-[2-(4-piperidyl)ethyl]indole in 1.2 l. CH2Cl2 and 50 g. NaHCO3 in 500 ml. H2O, the mixt. stirred 2 hrs. and worked up, the product in 300 ml. (CH2OMe)2 added dropwise to a stirred suspension of 25 g. LiAlH4 in 300 ml. (CH2OMe)2, and the mixt. stirred and refluxed 4 hrs., stirred overnight, 23 g. HCl salt, m. 231-3.degree., (could not be recrystd.), which is basified with Et2O-10% NaOH soln., and the isolated base (foam) treated with oxalic acid to give 17.5 g. 1-(2-indol-3-ylethyl)-4-[2-(2-methylindol-3-yl)ethyl]-piperidine oxalate, m. 165-9.degree. (decompn.). A mixt. of 15 g. 1-benzyl-3-[2-(4-pyridyl)ethyl]indole-HCl, 30 ml. H2O, 23 ml. EtOH, and 0.3 g. PtO2 is hydrogenated at 50 lb./in.2 (initial pressure) 20 hrs. and worked up to give 1-benzyl-3-[2-(4-piperidyl)-ethyl]indole, m. 51-3.degree. (pentane). A stirred mixt. of 5.2 g. of this, 1.9 g. finely-ground Na2CO3.H2O and 25 ml. iso-PrOH is refluxed while adding dropwise a soln. of 37 g. 3-(2-bromoethyl)-indole (III) in 10 ml. iso-PrOH, and the mixt. stirred and refluxed 18 hrs. and worked up to give 3.7 g. 1-(2-indol-3-ylethyl)-4-[2-(1-benzylindol-3-yl)ethyl]piperidine-HCl, m. 199-200.degree. (EtOH); similarly prepd. is the 1-Me analog, m. indefinite <80.degree.. I (2 g.) is added portionwise with stirring to a soln. prepd. from 150 ml. liq. NH3, 248 mg. Na and 1 crystal Fe(NO3)3.9H2O, after 1 hr. a soln. of 1.56 g. MeI in 10 ml. Et2O added dropwise, and the mixt. stirred 2 hrs. and worked up to give 1.2 g. 1,4-bis[2-(1-methylindol-3-yl)ethyl]piperidine, m. 124-4.degree. (AcMe). A soln. of 2.52 g. 5-methoxy-3-[2-(4-pyridyl)ethyl]-indole and 2.24 g. III in 50 ml. abs. EtOH is kept 1 week at room temp., 0.2 g. PtO2 added, and the mixt. hydrogenated at 50 lb./in.2 and 50.degree. 24 hrs. and worked up to give 1.6 g. 1-[2-(3-indolyl)ethyl]-4-[2-(5-methoxy-3-indolyl)ethyl]piperidine-HBr, m. 211-12.degree. (MeOH). To a vigorously stirred mixt. of 23 g. I in 350 ml. CHCl3 and 23 g. KHCO3 in 100 ml. H2O is added dropwise 23 g. 2-methylindol-3-ylglyoxyloyl chloride in 500 ml. EtOAc, and the mixt. kept 1 hr., and worked up to give 4-(2-indol-3-ylethyl)-1-(2-methylindol-3-ylglyoxyloyl)piperidine (IV), m. 202-3.degree. (EtOH); similarly prepd. in 73% yield is 4-[2-(2-methylindol-3-yl)ethyl]-1-(2-methylindol-3-

ylglyoxyloyl)piperidine, m. 228-9.degree. (EtOAc). IV (20 g.) is added portionwise to a stirred suspension of 10 g. LiAlH4 in 500 ml. dry (CH2OMe)2, and the mixt. refluxed 18 hrs. and worked up to give 9.2 g. 1-[2-(2-methylindol-3-yl)-ethyl]-4-[2-(3-indoly)ethyl]piperidine, m. 154-5.degree. (EtOAc); similarly prepd. in 76% yield is 1,4-bis[2-(2-methylindol-3-yl)-ethylpiperidine, m. 165-7.degree. (EtOAc). A soln. of 2.36 g. 2-methyl-3[2-(4-pyridyl)ethyl)indole and 2.24 g. III in 10 ml. MeCN is refluxed 16 hrs. and worked up to give 1-[2-(3-indolyl)-ethyl]-4-[2-(2'-methyl-3-indolyl)ethyl]pyridinium bromide hydrate, m. 145-7.degree. (aq. EtOH). Similarly prepd. is the 2'-isopropyl analog, m. 5.degree. (EtOH). To a stirred soln. of 2.6 g. piperazine in 100 ml. dry (CH2OMe)2 is added dropwise 4.2 g. II in 25 ml. (CH2OMe)2, and the ppt. worked up to give 4.3 g. 1,4-bis(3-indoleglyoxyloyl)piperazine (V), m. 360.degree. (HCONMe2-H2O). Similarly prepd. are the N,N'-bis(3-indoleglyoxyloyl) derivs. [m.p. and solvent (where other than aq. HCONMe2) given] of homopiperazine [330.degree. (decompn.)]; trans-2,5-dimethylpiperazine [361.degree.-2.degree. (decompn.), HCONMe2]; cis-2,5-dimethylpiperazine [337-9.degree. (decompn.), AcNMe2-H2O]; 1,2,3,4,-tetra-hydroquinoxaline [290.degree. (solvate)]; 2,6-dimethylpiperazine [342-3.degree. (decompn.)]; 2,3,5,6-tetramethylpiperazine.0.5H2O [322-4.degree.; and 2-methylpiperazine [348-50.degree. (decompn.)]; the N,N'-bis(2-methylindol-3-ylglyoxyloyl) derivs. of piperazine [345-6.degree. (decompn.)]; cis-2,5-dimethylpiperazine [342-3.degree. decompn.)]; the N,N'-bis(5-methoxyindol-3-ylglyoxyloyl) derivs. of cis-2,5-dimethylpiperazine [297-300.degree. (decompn.)]; piperazine [365.degree. (decompn.) (0.5 H2O); and 1,4-bis(5-bromoindol-3-ylglyoxyloyl)-piperazie (<360.degree.). LiAlH4 (1 g.) is added to a suspension of 1 g. V in 100 ml. dry (CH2OMe)2, and the mixt. stirred and refluxed 24 hrs. and worked to give 0.6 g. 1,4-bis(2-indol-3-ylethyl)piperazine (VI), m. 196-7.degree. (EtOH-H2O). Similarly prepd. are the N,N'-bis(2-indol-3-ylethyl) derivs. (m.p. given) of homopiperazine [107-8.degree. (benzene, then Et2O after purification via the HCl salt); trans-2,5-dimethylpiperazine [202-4.degree. (AcNMe2)]; cis-2,5-dimethylpiperazine [157-8.degree. (Et2O then aq. EtOH)]; 1,2,3,4-tetrahydroquinoxaline (175-6.degree.); 2,6-dimethylpiperazine [174-6.degree. (EtOH)]; 2,3,5,6-tetramethylpiperazine [80-105.degree. (fumarate monohydrate)], 2-methylpiperazine [100-7.degree. (aq. EtOH)]; the N,N'-bis[2-(2-methyl-3-indolyl)ethyl] derivs. of piperazine [240-3.degree. (aq. HCONMe2)]; cis-2,5-dimethylpiperazine [182-208.degree. (aq. HCONMe2)]; and 1,4-bis[2-(5-methoxy-3-indolyl)-ethyl]piperazine [210-11.degree. (aq. HCONMe2)]. VI (7.46 g.) is added to a stirred soln. prepd. from 1.1 g. Na and .apprx.500 ml. liq. NH3, 5.8 g. MeI in 100 ml. Et2O added dropwise to the stirred mixt., the NH3 evapd. overnight, and the mixt. worked up to give 7 g. 1,4-bis[2-(1-methyl-3-indolyl)ethyl]piperazine (VII), m. 129-31.degree. (EtOH); similarly prepd. are the following analogs (m.p. given) contg. instead of the 1-Me group: Et [125-7.degree. (EtOH)]; and PhCH2 [158-61.degree. (EtOAc)]. Also prepd. were the cis-2,5-piperazine analog of VII [81-4.degree. (hexane)]; and 1,4-bis[2-(1,2-dimethyl-3-indolyl)ethyl]-cis-2,5-dimethylpiperazine [176-8.degree. (aq. HCONMe2)]. VI is also prepd. by stirring a mixt. of 44.8 g. III, 8.6 g. piperazine, and 30.3 g. iso-Pr2NH in 200 ml. HCONMe2 18 hrs. at room temp. and working up.

IT **22547-36-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

RN 22547-36-0 CAPLUS

CN 1H-1,4-Diazepine, hexahydro-1,4-bis(1H-indol-3-yloxoacetyl)- (9CI) (CA INDEX NAME)